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annual report

July 1, 1970 - June 31, 1971

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PREFACE

The National Institutes of Health, a component of the Department of Health, Education, and Welfare, is the principal agency of the Federal government responsible for biomedical research, communication of biomedical knowledge, and education for the health professions.

To permit full dissemination of information on its responsibilities and accomplishments this Annual Report for Fiscal Year 1971 is published. Appropriate tables showing appropriations, grants and other extramural awards, and personnel levels have been included.

It is hoped this publication will serve as a ready reference volume for those concerned with NIH activities.

A handwritten signature in dark ink, reading "Robert Q. Marston, M.D.", written in a cursive style.

Robert Q. Marston, M.D.
Director

CONTENTS

THE NATIONAL INSTITUTES OF HEALTH	Page
Officers	ix
The Year in Review	1
Honors and Awards	2
Appointments	2
Facilities	3
Research Advances	3
National Cancer Institute	5
Support of Cancer Research	5
Viruses and Cancer	5
Chemicals and Cancer	6
Detection and Treatment	6
Immunology and Cancer	7
Molecular Biology and Cancer	8
National Eye Institute	9
Collaborative Research	9
Research Accomplishments	9
Cooperative Study	10
Reorganization	10
National Heart and Lung Institute	11
Extramural Research and Training	11
Collaborative Research and Development	11
Intramural Research	13
National Institute of Allergy and Infectious Diseases	15
Allergy and Immunology	15
Infectious Diseases	16
National Institute of Arthritis and Metabolic Diseases	18
Arthritis and Rheumatoid Diseases	18
Diabetes and Epidemiological Research	18
Hereditary Metabolic Diseases	18
Endocrinology	19
Kidney Diseases and Artificial Kidneys	19
Digestive Diseases and Nutrition	20
Diseases of the Blood	20
National Institute of Child Health and	
Human Development	21
Population Research	21
New Contraceptive Methods	21
Medical Effects of Current Birth Control Methods	21
Population Research in the Social Sciences	22
Research and Training	22
Child Health	22

CONTENTS—Con.

	Page
Identification of Genetic Defects in the Fetus	22
Growth and Nutrition	23
Mental Retardation	23
Adult Developing and Aging	23
National Institute of Dental Research	24
Dental Caries	24
Target for the 70's	24
Dental Repair, Biomaterials	25
Periodontal (Gum) Disease	25
Pain and Anesthesiology	25
National Institute of Environmental Health Sciences	26
Mutagenesis	26
Screening of Chemicals for Mutagenesis	26
Developing Techniques for Working in Mutagenesis	26
Teratogenesis-Carcinogenesis	27
Microwave Exposure System	27
CNS Toxicity of Metals	27
National Institute of General Medical Sciences	29
Administration	29
Research Progress	29
Genetics	29
Fundamental Sciences	30
Automated Clinical Laboratories	30
Pharmacology-Toxicology	31
Trauma	31
National Institute of Neurological Diseases and Stroke	32
Research Trends	32
Disorders of the Aged	32
Sclerosing Disorders	33
Spinal Cord Injuries	34
Clinical Center	35
Patient Load and Care	35
Diagnostic Radiological Services	35
Automated Laboratory Procedures	36
Elective Courses	36
Associate Training Program	36
Division of Biologics Standards	37
Diploid Cell Lines	37
Hepatitis Research	37
Division of Computer Research and Technology	39
Facilities and Services	39

CONTENTS—Con.

	Page
Systems Development	39
Research Developments	39
Education	40
Division of Research Grants	41
Division of Research Resources	42
Biotechnology Resources	42
General Clinical Research Centers	42
Animal Resources	42
General Research Support	43
Division of Research Services	44
Environmental Services	44
Biomedical Engineering and Instrumentation	44
Animal Programs	44
Library Services	45
Medical Arts and Photography	45
The Fogarty International Center	46
Scholars-in-Residence	46
Conferences and Seminars	46
Bilateral Agreements for Cooperation	46
Geographic Health Studies	47
Bureau of Health Manpower Education	48
Administrative Changes	48
Legislative Developments	48
Division of Allied Health Manpower	49
Allied Health Training	49
Public Health Training	49
New Special Activities	49
Division of Dental Health	50
Caries Prevention	50
TEAM	50
Dental Manpower Development Center	50
"Dr. Dial"	50
Continuing Dental Education	51
Grant Awards	51
Division of Manpower Intelligence	51
Accomplishments	51
Contracts	51
Division of Nursing	52
Aid to Students	52
Research and Research Training	52

CONTENTS—Con.

	Page
State Planning and Manpower Studies	53
Division of Physician and Health Professions Education	53
New Special Activities	53
Educational Improvement Awards	53
Student Assistance	53
Health Professions Educational Facilities	54
National Library of Medicine	55
Library Operations	55
Lister Hill National Center for	
Biomedical Communications	56
Specialized Information Services	56
National Medical Audiovisual Center	56
Extramural support	57
 APPENDICES	
Appropriations	58
Grants and Awards	60
Employment	61

NATIONAL INSTITUTES OF HEALTH

Officers

as of

July 1, 1971

Robert Q. Marston, M.D.	Director, National Institutes of Health
John F. Sherman, Ph.D.	Deputy Director, National Institutes of Health
Robert W. Berliner, M.D.	Deputy Director for Science
Ronald W. Lamont-Havers, M.D.	Associate Director for Extramural Research and Training
Robert W. Berliner, M.D.	Associate Director for Direct Research
Leon Jacobs, Ph.D.	Assistant Director for Collaborative Research
Thomas J. Kennedy, Jr., M.D.	Associate Director for Program Planning and Evaluation
Thomas C. Chalmers, M.D.	Associate Director for Clinical Care
Leonard D. Fenninger, M.D.	Associate Director for Health Manpower
Richard L. Seggel	Associate Director for Administration
Storm Whaley	Associate Director for Communications
Irving Goldberg	Director of Information
Carl G. Baker, M.D.	Director, National Cancer Institute
Carl Kupfer, M.D.	Director, National Eye Institute
Theodore Cooper, M.D.	Director, National Heart and Lung Institute
Dorland J. Davis, M.D.	Director, National Institute of Allergy and Infectious Diseases
G. Donald Whedon, M.D.	Director, National Institute of Arthritis and Metabolic Diseases
Gerald D. LaVeck, M.D.	Director, National Institute of Child Health and Human Development
Seymour J. Kreshover, D.D.S.	Director, National Institute of Dental Research
David P. Rall, M.D.	Director, National Institute of Environmental Health Sciences
DeWitt Stetten, Jr., M.D.	Director, National Institute of General Medical Sciences
Edward F. MacNichol, Jr., Ph.D.	Director, National Institute of Neurological Diseases and Stroke
Thomas C. Chalmers, M.D.	Director, Clinical Center
Roderick Murray, M.D.	Director, Division of Biologics Standards
Arnold W. Pratt, M.D.	Director, Division of Computer Research and Technology

Stephen P. Hatchett, Ph.D.	Director, Division of Research Grants
Thomas G. Bowery, Ph.D.	Director, Division of Research Resources
William B. DeWitt, Ph.D.	Director, Division of Research Resources
Milo D. Leavitt, Jr., M.D.	Director, Fogarty International Center for Advanced Study in the Health Sciences
Kenneth M. Endicott, M.D.	Director, Bureau of Health Manpower Education
Robert M. Bucher, M.D.	Deputy Director
Charles H. Boettner, M.D.	Associate Director
Daniel F. Whiteside, D.D.S.	Associate Director
Eugene A. Confrey, Ph.D.	Associate Director for Program Plan- ning and Evaluation
Thomas D. Hatch	Acting Director, Division of Allied Health Manpower
Harry W. Bruce, Jr., D.D.S.	Director, Division of Physician and Health Professions Education
Jessie M. Scott	Director, Division of Nursing
John C. Greene, D.M.D.	Director, Division of Dental Health
William A. Lybrand, Ph.D.	Director, Division of Manpower Intel- ligence
Martin M. Cummings, M.D.	Director, National Library of Medicine
G. Burroughs Mider, M.D.	Deputy Director
Charles F. Bridgman, Ph.D.	Associate Director for Audiovisual Tele- communications and Director of Na- tional Medical Audiovisual Center
Albert Fejner	Associate Director for Research and De- velopment and Director of Lister Hill National Center for Biomedical Com- munications
Henry M. Kissman, Ph.D.	Associate Director for Specialized In- formation Services
Leroy L. Langley, Ph.D.	Associate Director for Extramural Pro- grams
Joseph Leiter, Ph.D.	Associate Director for Library Opera- tions
Ralph A. Simmons	Associate Director for Computer and Engineering Services

The National Institutes of Health

The Year In Review

The National Institutes of Health during Fiscal Year 1971 was able to consolidate gains in knowledge contributing to improved national health. The trend of events in administration of programs in biomedical research, in education of health professionals, and in rapid dissemination of new knowledge provided opportunities for re-evaluation in a number of areas.

It was a year of significant achievement on several salients, despite unusual problems in financing because amounts budgeted for use during the year were not determined until March. Continuation of the climate of austerity, in which funding gains were approximately matched by inflationary cost increases, influenced operations as in other recent years.

By contrast, the likelihood of substantial expansion in the scope of two important fields, cancer research and health manpower education, brought promise of increased momentum and a more vigorous approach in planning.

The President, in his Health Message to Congress on February 18, outlined a comprehensive policy which included recommendations for expanded cancer and sickle cell anemia research. Later he asked Congress to "establish a cancer-cure program within the National Institutes of Health," which would have independent budgetary status and a director appointed by and responsible directly to the President. He included an extra \$100 million in the Fiscal Year 1972 budget for cancer research, saying he would ask for whatever additional funds could be effectively used to conquer cancer. For sickle cell anemia research and treatment he proposed an increase up to \$6 million.

The anticipated expiration on June 30 of legislative authority for two important aspects of health manpower education required extensive attention by NIH staff. The two, the Health Professions Education Assistance Act, and the Nurse Training Act, were given

important new emphasis in budgets proposed for the coming Fiscal Year (1973).

The Bureau of Health Professions Education and Manpower Training was reorganized during the year and renamed the Bureau of Health Manpower Education. The Division of Research Resources, assigned to the Bureau in 1969, was reassigned to independent status among NIH's research divisions.

Honors and Awards

Secretary Elliot L. Richardson presided at the Annual DHEW Honor Awards Ceremony in the Jack Masur Auditorium in the Clinical Center at which NIH scientist-administrators were honored. Dr. John F. Sherman, Deputy Director of NIH, and Dr. Donald S. Frederickson, Director of Intramural Research for the National Heart and Lung Institute, were presented with Distinguished Service Awards. Three members of the Public Health Service Commissioned Corps received Distinguished Service Medals: Assistant Surgeon General Dorland J. Davis, Director of the National Institute of Allergy and Infectious Diseases; Dr. Herbert G. Stoenner, Director of the NIAID Rocky Mountain Laboratory; and Dr. Robert M. Channock, Chief of the NIAID Laboratory of Infectious Diseases.

Secretary Richardson also recognized at that ceremony two other scientists who previously had been recipients of national recognition. These were: Dr. Robert J. Huebner, National Cancer Institute virologist, who received during the year both the National Medal of Science from President Nixon and the Rockefeller Public Service Award, and Dr. George J. Todaro, also of the National Cancer Institute, who received one of the Ten Outstanding Young Men of the Year Awards from the Junior Chamber of Commerce of the United States.

Other important awards during the year went to Dr. Robert W. Berliner, Deputy Director for Science, who received the American Heart Association's 1970 Research Achievement Award, and to Dr. Frederickson, who was awarded the 1971 *Modern Medicine* Award for Distinguished Achievement.

Appointments

Dr. DeWitt Stetten, Jr., Dean of the Rutgers University Medical School, and formerly Director of Intramural Research in the National Institute of Arthritis and Metabolic Diseases, was appointed Director of the National Institute of General Medical Sciences.

In another appointment Dr. David P. Rall was named Director of the National Institute of Environmental Health Sciences to succeed Dr. Paul Kotin, who resigned to become Vice President for Health Sciences at Temple University. Dr. Rall previously was associate scientific director of the National Cancer Institute, supervising experimental therapeutic efforts.

Reflecting the increased emphasis on contract financing of research and in accordance with recommendations of a study made by a joint Office of the Secretary-NIH team, an Office of Contracts and Grants was established and assigned to the Associate Director for Administration.

Facilities

In February, the National Institute of Neurological Diseases and Stroke opened its new controlled-access laboratories in Building 36 for the study of infectious diseases in newborn children and in the fetus. In June, a new primate facility and two research buildings for the National Institute of Mental Health were dedicated at the NIH Animal Center at Poolesville, Md. And in March a cluster of four new buildings was dedicated at the National Institute of Environmental Health Sciences in Research Triangle Park, N.C.

In November, the National Institute of Arthritis and Metabolic Diseases and the National Institute of Neurological Diseases and Stroke celebrated their 20th anniversaries.

Activity was expanded under the Equal Opportunity and Upward Mobility Programs, and several conferences were conducted by Institutes, Bureaus and Divisions and other specific steps taken to resolve problems of minority employees. In addition, NIH implemented the DHEW Affirmative Action for Women by appointment of a Coordinator of the Federal Women's Program.

Research Advances

Advances were made in several areas of basic research and clinical medicine.

Two university teams of research scientists receiving NIH support reported that certain tumor viruses with a ribonucleic acid core contain an enzyme that in at least some instances reverses the pattern of genetic information channeling, using ribonucleic acid, or RNA, as a blueprint for synthesis of deoxyribonucleic acid, or DNA. Previously it had been thought that DNA invariably was the master chemical in living cells and RNA the servant. The reports were by Drs. Howard M. Temin and Satoshi Mizutani of the Univ-

ersity of Wisconsin and Dr. David Baltimore of the Massachusetts Institute of Technology. Their results were confirmed by Dr. Sol Spiegelman, another NIH grantee, at Columbia University. The findings open up new approaches to understanding of cancer causation and prevention and in the transmittal of hereditary information.

Two NIH intramural scientists, Dr. Roscoe O. Brady of the National Institute of Neurological Diseases and Stroke and Dr. Peter T. Mora of the National Cancer Institute, discovered a biochemical defect—greatly reduced activity or possibly entire lack of the enzyme, amino-sugar transferase—in cells that have recently been transformed by DNA viruses into cancer cells. This was the first finding of a specific biochemical change associated with cell transformation by tumor-causing viruses.

Two University of California at San Francisco scientists, Dr. C.H. Li and Dr. D. Yamashiro, whose research has been supported by NIH for more than 17 years, achieved synthesis of human growth hormone. The team previously had isolated and identified the hormone. The synthesis is expected to have enormous implications for treatment of dwarfism, gigantism, obesity, diabetes and other conditions.

A team of scientists of the National Institute of Neurological Diseases and Stroke discovered that an experimental drug, frequently used in the past to treat patients with disorders accompanied by elevated levels of blood potassium, is successful in combating a baffling neurological disease. Drs. W. King Engel, Robert C. Griggs and Jerome S. Resnick found improvement was dramatic in patients with hypokalemic periodic paralysis, a disorder of unknown cause associated with low levels of natural potassium in the body, which afflicts hundreds of persons in this country and abroad.

Another NIH grantee, Dr. Donald A. Gerber of Downstate Medical Center, New York, reported successful reduction of symptoms in rheumatoid arthritis patients by administering large daily doses of histidine, an amino acid found in most proteins.

National Cancer Institute

Support of Cancer Research

Federal support of cancer research increased during Fiscal Year 1971 to a greater degree than in any year since the National Cancer Institute was established in 1937. The expanded funding required the Institute to emphasize projections of activity for a minimum of five future years.

The trend began when an increase of \$20 million for virus-cancer work was included in the fiscal 1971 appropriation request of \$202,383,000. To this the Congress added \$28 million, putting the Institute approximately \$50 million over its previous operating level. The President also called for a national commitment to the conquest of cancer and asked that an additional \$100 million be made available. This was appropriated as a supplement to the FY 1971 budget for use in 1972 and 1973. The Administration further proposed legislation to establish a new Conquest of Cancer Agency as an independent agency within the National Institutes Of Health.

Anticipating growth to an operating level approaching \$1 billion by 1976, Institute staff intensified planning and outlined in broad terms the scientific and management aspects of a more comprehensive research effort. Two meetings with expert consultants from within and outside the Government were convened to obtain advice on how to mount an attack of unprecedented dimensions on key cancer problems. The first day-long session with a group of eminent scientists was held in March and a similar meeting with prominent research administrators in May. An additional series of meetings of approximately 50 groups of scientists and physicians was planned for the Fall of 1971.

Meanwhile, a series of staff conferences was conducted to consider the relationship to NIH of the proposed new Conquest of Cancer Agency.

Viruses and Cancer

Evidence of the virus causation of certain types of human cancer continued to accumulate.

In the September 1970 issue of the *Journal of the National Cancer Institute*, Dr. Laure Aurelian and her colleagues at the Johns Hopkins School of Medicine reported additional evidence of the implications of Type 2 herpes virus in cervical cancer. She presented immunologic evidence that the virus was present in cells she obtained from 95 percent of women with very early, pre-cancer-

ous "atypical" cells of the cervix, as well as in 100 percent of cells from women with advanced invasive cancer of the cervix.

Scientists supported by NCI's Special Virus Cancer Program reported new evidence of a virus cause of breast cancer, a principal cause of cancer death in women. An international team of scientists found particles structurally similar to those of the mouse mammary tumor virus in milk from Parsi women in India and in American women with a high risk of breast cancer. Later the characteristic enzyme "reverse transcriptase" was detected in the milk of these women.

Chemicals and Cancer

In an effort to identify cancer-causing substances more efficiently, the NCI initiated a project at the Stanford Research Institute of Menlo Park, Calif., to establish priorities for screening in laboratory animals of the countless new chemicals introduced into the human environment each year, in addition to familiar compounds. Industrial chemicals, foodstuffs, air and water pollutants are among the thousands of materials being considered under the study.

Detection and Treatment

Evaluation of the carcinoembryonic antigen (CEA) test for detection of early cancer of the large intestine and rectum was begun under NCI contract.

Early detection of breast cancer among women screened with an X-ray technique called mammography combined with clinical examinations resulted in 40 percent fewer deaths due to breast cancer than among an unscreened control group. Results of the NCI-supported study were published in April 1971.

In November 1970 Dr. Robert C. Gallo of NCI reported on test tube experiments in which a derivative of the antibiotic rifampicin inhibited completely an enzyme found in the white blood cells of leukemia patients. The enzyme, "reverse transcriptase," had been reported earlier in the year to be associated with certain viruses that cause cancer in animals.

NCI grantees Drs. Max M. Burger and Kenneth D. Noonan reported on experiments with trypsinized Concanavalin A (Con A), a protein obtained from the jackbean plant. They found that it adhered to and clumped malignant mouse cells growing in tissue culture; by covering up an exposed layer of surface receptors on these cells, Con A restored their growth pattern to the normal state of "contact inhibition."

Two meetings of importance were sponsored by NCI. The first advised practicing physicians on drugs mithramycin (sometimes useful in inoperable cancer of the testes) and o,p'-DDD (a drug related to DDT, helpful in some adrenal cancers). The second meeting aimed at improving prospective, randomized, controlled studies of cancer therapy.

For certain patients with Hodgkin's disease, a cancer of the lymph system common in young adults, high-dose, extended-field radiotherapy was reported useful. Among patients with early or locally advanced Hodgkin's disease, the treatments resulted in a 5-year survival rate of greater than 90 percent, Dr. Ralph Johnson of NCI reported.

In far advanced Hodgkin's disease, drug therapy is the preferred treatment. In August 1970 NCI scientists reported that a 4-drug treatment more than doubled the survival time of patients who responded. Using a regimen including the drugs vincristine, procarbazine, prednisone and an alkylating agent, a complete remission rate 4 times greater than usual was achieved.

In another type of lymph system cancer, lymphosarcoma, a high-dose 3-drug combination developed by NCI scientists produced a higher survival rate than treatment previously reported. Complete remissions were achieved in 57 percent of the patients studied; 73 percent of them were alive 2 years after treatment.

Immunology and Cancer

Efforts to stimulate cancer patients' natural defenses against their disease progressed during the year; a vaccine against tuberculosis called BCG was an effective tool in stimulating the immune response.

Dr. Donald L. Morton of NCI reported using BCG in treating melanoma, an often fatal cancer that may develop from a pre-existing mole. Dr. Morton reported on the treatment of eight patients with inoperable melanoma by inoculations of BCG directly into the melanoma nodules, achieving temporary tumor regressions in five patients; one remained free of disease two years following treatment.

NCI scientists Drs. Berton Zbar, Herbert J. Rapp, Gerald L. Bartlett and colleagues reported on experiments in which tumor cells obtained from guinea pigs were mixed with BCG, and the mixture was injected into the skin of unimmunized guinea pigs. An inflammatory response to BCG occurred, and there was no progressive tumor growth. Without BCG, the tumors grew progressively

and killed the animals. Later experiments showed that immunity could be induced in the animals when they were inoculated with BCG and as many as 1.5 million tumor cells. The scientists suggest that improved immunity to tumors may be possible by mixing some of a patient's own cancer cells with BCG and then re-inoculating them into the individual.

Molecular Biology and Cancer

Confirmation of a newly discovered enzyme associated with RNA tumor viruses—"reverse transcriptase"—was reported by an NCI-supported scientist. Dr. Sol Spiegelman found the enzyme in RNA viruses associated with tumors of mice, cats, monkeys and birds.

Evidence of the enzyme was reported in human leukemic cells by an NCI scientist, Dr. Robert C. Gallo; in May 1971 investigators discovered the enzyme in milk samples from women, both American and Indian, with family histories of breast cancer.

In February 1971 the discoverer of the enzyme, Dr. Howard M. Temin, proposed his "provirus theory" on the cancerous and normal development of cells. The NCI grantee postulated the existence during fetal life of a "provirus"—a missing link between virus and gene. He suggested it may allow flexible transfer of genetic information during cell differentiation, thus varying the genetic potential of cells.

Earlier, in September 1970, Dr. Robert J. Huebner of NCI postulated that an inherited cancer gene present even before birth could also be a growth factor in the developing embryo. He had detected inherited genetic material, common to a group of viruses that cause cancers in mice, chickens, hamsters and cats, through its "foot-prints" in healthy embryos of both laboratory bred and wild mice. Dr. Huebner's hypothesis suggests that a potential cancer gene is present in all normal cells from conception; by contrast, Dr. Temin suggests that a potential cancer gene is formed in body cells by provirus transfer during embryonic development.

National Eye Institute

During Fiscal Year 1971, the National Eye Institute completed development of a fully-functioning, independent program of vision research within NIH. Important additions to staff, expansion of advisory resources, reorganization of programs, and significant progress in vision research highlighted the year.

Collaborative Research

With significant budetary increases, the Institute was able to award its first contracts for vision-related research and development. Among the collaborative projects underway are: investigations of drug therapy in the treatment of glaucoma (Yale and Washington Universities); development of diagnostic techniques for diseases of the retina (Boston University); studies of the impact of chromosomal defects on the development of the human eye; and the development of a biomedical image processing system to collect and analyze morphological data from the eye and eye-related structures.

Research Accomplishments

Through grants, NEI supports over 400 research projects at universities, hospitals, research institutes, and other public and private nonprofit institutions in addition to conducting its own intramural research program. Significant progress against visual disorders in four major areas was made during the year: disorders of the retina and its underlying layer, the choroid; inflammatory disease; glaucoma; and strabismus.

Improved diagnosis of retinal and choroidal disorders has become possible through the use of fluorescein angiography, a technique which permits direct observation of bloodflow through ocular vessels. NEI grantee exploration of the efficiency of cryosurgery (freezing) in reattaching the retina could have profound effects on reducing the cost of medical care associated with the management of retinal detachment.

Research on the retina in the Institute's own laboratories resulted in the first description of color vision at the level of a single nerve cell. An important development in the management of ocular inflammatory disease was the demonstration that hydrophilic (soft) contact lenses can aid in healing superficial, sterile corneal ulcers which would otherwise require surgery. In an analysis of normal and damaged corneas, an NEI grantee isolated the

enzyme collagenase as a destructive agent present in injured corneas, but absent in normal ones.

Promise for better control of elevated intraocular pressure which may lead to glaucoma lies in grantee efforts to enhance the effect of the hormone norepinephrine on the sympathetic nerves of the eye—a therapy which may lower pressure. Although in the past primary open-angle glaucoma has been considered rare in adolescents and young adults, an Institute-supported analysis of young glaucoma patients revealed that 25 percent probably did have this form of the disease. Therefore investigators advised that tonometry should be performed on all patients old enough to cooperate, particularly those with a family history of glaucoma.

Research in strabismus identified for the first time a group of cells in the visual cortex of macaque monkeys believed to link the visual fields from each eye, creating the ability for three-dimensional vision.

Cooperative Study

The Institute launched a collaborative clinical study on the treatment of diabetic retinopathy, an eye disease rapidly becoming the leading cause of new adult blindness in many States. Scientists from 11 institutions will pool resources to evaluate current therapy used in treating diabetic retinopathy and to study the natural history of the disease. Over 1,600 patients will be enrolled at participating clinical centers during the first two years of the project.

Reorganization

Reorganization within the Office of the Director included establishment of an Office of Biometry and Epidemiology charged with conducting mathematical and statistical research on vision and its disorders. The Office of the Director of Intramural Research was created to administer the activities of the newly established Laboratory of Vision Research and the Clinical Branch, which replaced the former Ophthalmology Branch.

The Institute's Eye Clinic in the NIH Clinical Center was renovated and enlarged, permitting a greatly expanded program of intramural clinical research. A Vision Care Program to place patients who do not require full-time hospital care in off-campus housing further increased the Institute's patient capacity while reducing the average cost of medical care. To advise the Institute on scientific matters relating to the Intramural Program, a Board of Scientific Counselors, comprised of six distinguished vision research scientists, was created.

National Heart and Lung Institute

Extramural Research and Training

During Fiscal Year 1971, NHLI supported 1,539 research grants totalling \$116,771,000 for studies in the following major disease categories: arteriosclerosis, including coronary heart disease and cerebrovascular disease; cardiac diseases, including congenital and rheumatic heart disease; hypertension and kidney disorders; pulmonary diseases, especially emphysema and chronic bronchitis; and thrombotic and hemorrhagic diseases.

A new attack on high-priority problems was launched with the award of 34 grants totalling \$16.4 million for the establishment of Specialized Centers of Research (SCORs) at 29 medical facilities throughout the country. Each SCOR will concentrate manpower and resources on high-priority problems in one of the following disease areas: arteriosclerosis (13 SCORs), pulmonary disease (11 SCORs), thrombosis (5 SCORs), and hypertension (5 SCORs). The goal is to develop new knowledge relevant to prevention, diagnosis, and clinical management of these disorders and hasten its clinical application.

The Institute also awarded 390 training grants totalling \$17,727,038 and 325 fellowships and career development awards totalling \$6,553,536 to: 1) expand and improve training provided to medical students and 2) support advanced training of students and graduates seeking research, teaching, or clinical careers.

A series of Pulmonary Academic Awards to schools of medicine or osteopathy was initiated to improve training programs and to foster academic careers in the pulmonary-disease field. Four grants totalling \$199,236 were awarded.

Collaborative Research and Development

The Collaborative Research and Development Program provides research contracts for highly targeted research. Many of these projects directly complement, but do not duplicate, studies supported under regular research grants.

The Medical Devices Applications Program supported 84 contracts totalling \$9.2 million during fiscal 1971 for studies to develop and evaluate heart-assist devices and total mechanical replacements for hearts damaged beyond repair. Also under development are devices and techniques for temporary maintenance of adequate blood oxygenation during acute respiratory crises result-

ing from chronic lung diseases, such as emphysema, or hyaline membrane disease in newborn infants. Significant developments during the past year include:

- Several new materials and surfaces that do not promote clotting when used in implanted devices.
- An improved capillary membrane oxygenator for use with heart-lung machines during prolonged open heart procedures or for temporary respiratory support in patients with acute respiratory failure.
- Several engines, powered by electricity or radioisotopes, that are compact enough to be totally implantable and powerful enough to drive a heart-assist device or artificial heart.

The *Myocardial Infarction Branch* awarded 36 contracts totalling \$7,022,662 for research directed toward reduction of death and disability from acute heart attacks and their complications. This included continued support for 9 Myocardial Infarction Research Units (MIRUs) previously established for the intensive clinical study of heart-attack patients during the acute phase of their illness.

Other research included:

- Studies on the onset of acute heart attacks and sudden cardiac death. Goals include the identification of "trigger" factors that precipitate the acute episode; the definition of host or environmental factors that increase risk of potentially lethal attacks; identification of physiological factors that contribute to a rapidly fatal outcome after onset; and development of practical treatments for the earliest stages of acute heart attacks.
- Studies seeking means of protecting heart muscle against the destructive consequences of blood deprivation, thereby reducing the extent and severity of heart damage.

The *National Blood Resource Program* during fiscal 1971 supported 79 contracts totalling \$5,687,720. Research included:

- Clinical trials evaluating and comparing three promising forms of treatment for sickle cell crises. These painful, disabling episodes pose an ever-present threat to the estimated 50,000 American Negroes afflicted with sickle cell anemia.
- Pilot studies to determine whether the clot-dissolving agent urokinase is useful in the clinical management of acute heart attacks.
- Development of techniques for prenatal detection of hereditary blood diseases such as hemophilia.

- Development of more sensitive and reliable techniques for identifying hepatitis virus in blood and blood products and techniques for removing it.
- Development of procedures for improving the yield of antihemophilic factor precipitated from plasma by the freeze-thaw technique.
- A systematic study of blood banking practice and its problems.

The *Lipid Metabolism Branch*, established during 1971, is responsible for contract-supported research aimed at prevention of premature atherosclerosis through identification and treatment of those rendered highly susceptible by blood-lipid abnormalities. These abnormalities, called hyperlipoproteinemias, can be readily identified by lipoprotein analysis or other simpler techniques. The associated blood-lipid problem usually can be improved or completely corrected by appropriate therapeutic diets supplemented, as necessary, with specific lipid-lowering agents.

During fiscal 1971 the Branch awarded 7 contracts totalling \$2.6 million for the establishment of 6 Lipid Research Clinics and a Central Patient Registry and Coordinating Center. Among projects to be undertaken by these clinics are:

- Studies on the prevalence of the several types of hyperlipoproteinemias in the U.S. population, with emphasis on the nature and frequency of heritable forms.
- Assessment of the risk of atherosclerosis and its consequences associated with hyperlipoproteinemia.
- Evaluation of the effectiveness of reducing blood lipids in averting atherosclerosis, delaying the onset of overt symptoms, or bringing about regression of existing atherosclerotic deposits.

In addition, the Lipid Research Clinics will provide assistance and guidance to practicing physicians.

Intramural Research

The 11 intramural laboratories and branches conduct basic and clinical studies on the cardiovascular system and the diseases that afflict it. Among significant accomplishments reported were:

- Development of an electro-optical device, called the "Optisat", that provides continuous measurements of blood-oxygen levels during the use of heart-lung machines or respiratory assist devices.

- The finding that familial Type II hyperlipoproteinemia—one of the most common and most dangerous of the hereditary blood-lipid disorders—can be diagnosed from birth and effectively treated during childhood. The elevated cholesterol levels can be reduced by therapeutic diets supplemented, if necessary, by the cholesterol-lowering drug cholestyramine.
- The finding that radar kymography, a special fluoroscopic technique developed at NHLI, provides a reliable, non-invasive means of evaluating heart-muscle contractility.
- The finding that diazepam, a tranquilizer and muscle relaxant, is an unusually safe and useful sedative for patients recovering from heart surgery. Unlike many tranquilizers, diazepam does not depress heart function and may even improve it.

National Institute of Allergy and Infectious Diseases

Allergy and Immunology

During the past few years, rapid and spectacular advances in immunology have yielded leads which are now ready for translation into improved methods of diagnosing and treating allergic patients. The National Institute of Allergy and Infectious Diseases (NIAID) therefore is increasing its emphasis on allergic diseases and has initiated a new program of research by creating seven Allergic Disease Centers.

Laboratory research in immunology is already in progress at these Centers. The new grants permit related clinical studies of allergic individuals, primarily out-patients.

Problems to be studied include: chemical substances (mediators) that induce activity in reactive tissues and cause allergic symptoms; therapeutic approaches to allergies and asthma; immunologic, pharmacologic, environmental, and psychologic factors contributing to symptoms of asthma; and the role of respiratory infections in development of asthma.

Studies at the Centers will be similar to investigations by NIAID grantees who found a chemical mediator of muscle activity in nasal secretions of patients allergic to ragweed. This compound appeared immediately after the individuals were challenged with ragweed pollen—a fact which suggests that formation of the substance may play a role in the development of the allergic reaction and that, if ways can be found to block its formation, patients may be relieved of some symptoms.

Research progress also promised help for the millions who suffer from conditions (other than allergy) in which an abnormal immune response plays an important role. In the NIH Clinical Center, for example, NIAID physicians have studied patients with a fungal infection known as chronic mucocutaneous candidiasis. Two types of defects in the lymphocytes (disease-fighting white cells) of the patients have been identified and massive transfusions of normal lymphoid cells from genetically identical donors have been successful as treatment. Other candidiasis patients have been given “transfer factor”—a little understood substance obtained from immune lymphocytes—and early results are encouraging.

Infectious Diseases

A research attack on an old enemy—influenza—is being prepared by a committee of experts who are helping NIAID devise strategies to cope with the pandemic expected in the late 1970's. In a series of conferences, the scientists are reviewing new information on the antigenic composition of the influenza virus and the significance of these antigens. Scientists now believe it will be possible to overcome the problem of periodic changes which occur naturally in influenza virus strains and have made necessary to produce "tailor-made" vaccines for strains prevalent at any given time.

Along with other investigators, NIAID scientists and grantees have been following developments in hepatitis. One form of this disease, transmitted by blood, occurs in many drug addicts and in perhaps 1 percent of patients following transfusion.

Until recently, it was impossible to identify blood carrying the hepatitis virus. Now, however, scientists have found a substance—called Australia or hepatitis-associated antigen (HAA)—whose presence indicates that the blood is likely to transmit infection.

Several methods have been developed to detect HAA and antibody to HAA. NIAID and other NIH scientists modified one of the most sensitive procedures, a radioimmunoassay technique, and used it to test sera from several population groups. The investigators found antibody to HAA rather frequently in the blood of persons with no history of hepatitis or drug addiction. This evidence suggests that unrecognized or subclinical HAA-positive hepatitis, transmitted by a non-parenteral route, may be endemic in the United States.

Procedures for large-scale isolation of well-characterized and highly-purified HAA (needed for biochemical studies and for the production of standardized animal antisera) have been worked out by scientists at the Rockville Laboratory of the Molecular Anatomy Program—a cooperative endeavor of the NIAID and the Division of Biology and Medicine, U.S. Atomic Energy Commission. They also found that the isolated HAA antigen consists of at least two proteins, or sub-types—a fact which helps explain the difficulty in preparing standardized reagents.

Some of NIAID's most exciting work in virology during the year was in connection with the so-called "slow viruses." Two of these—visna and progressive pneumonia virus—cause slowly evolving disease in sheep, eventually resulting in death of the animals. NIAID scientists showed that, in tissue culture, these two viruses also transform cells which, when injected in newborn or x-irradiated

laboratory animals, cause tumors. These findings—linking slow viruses and tumors—are believed to have important implications for both viral carcinogenesis and slow virus infections.

Work on Venezuelan equine encephalitis (VEE) at NIAID's Middle America Research Unit (MARU) in Panama resulted in data of enormous practical value to public health and agricultural officials confronted with an VEE epidemic in the southwestern region of the United States. MARU scientists, who had just completed a survey of a 1970 VEE outbreak in Costa Rica reported that (1) deaths of horses from the disease were independent of sex or age, (2) human infection ceased shortly after equine infection was brought under control, and (3) the crabhole mosquito, *Deinocerites psuedis*, probably was involved in transmission of the disease. The MARU investigators also found the experimental vaccine (strain TC-83) highly protective.

The search for agents active against bacterial strains that are resistant to present antimicrobials is constantly turning up new investigational drugs. One of these, carbenicillin, was reported by NIAID grantees and others as effective against gram-negative bacterial infections increasingly common in hospital patients. However, carbenicillin, a semi-synthetic penicillin, usually must be given in large doses and research is needed on the upper limits of its toxicity. It is recommended, at present, for use in selected situations only.

Both NIAID grantees and intramural scientists reported progress against the chronic parasitic disease, schistosomiasis, which afflicts 200 million persons in tropic and semi-tropic areas. NIAID grantees found that, in certain monkeys, infection with the parasite causing schistosomiasis produces bladder and urinary effects much like those in man. In similar work at NIAID, scientists produced urinary schistosomiasis in several species of monkeys and baboons, and also observed carcinoma of the urinary bladder in two monkeys infected with the parasite, *Schistosoma haematobium*. This finding is of particular importance since, in some countries, human schistosomiasis is believed to lead to bladder cancer.

National Institute of Arthritis and Metabolic Diseases

Arthritis and Rheumatoid Diseases

The likelihood that rheumatoid arthritis (RA) is initiated by an autoimmune reaction, in which the body overreacts to proteins originating within its own tissues, is undergoing intensive study. Such immune processes may be triggered by changes brought about by an infectious agent or agents. Virus-like particles have been found in the affected kidney tissues of patients with systemic lupus erythematosus (SLE), a connective-tissue disease related to RA. Although this finding does not establish a viral cause for SLE, presence of the particles is of diagnostic importance and further study may shed light on the infectious aspects of the cause of rheumatoid disease.

Diabetes and Epidemiological Research

The rising incidence of diabetes and the fact that it ranks eighth on the list of diseases causing death make continued research an unceasing obligation.

A principal goal in diabetes research is understanding the basic impairment of insulin action, and why the body is unable to utilize carbohydrates normally for energy expenditure and storage. Recent research has suggested that a pancreatic hormone other than insulin, glucagon, may also play an important role. It has been found that diabetes is characterized by a continuous state of glucagon excess, which, it is proposed, may exaggerate the consequences of insulin insufficiency and may unfavorably influence blood sugar level control.

In epidemiological studies of the Pima Indians of Arizona, scientists have confirmed that the symptoms and signs of diabetes, including eye and kidney damage, are correlated with the unusually high prevalence of abnormal glucose tolerance. A clinical research section now has been established at the new Phoenix Indian Medical Center to intensify Institute studies of diabetes, arthritis and gallbladder disease.

Hereditary Metabolic Diseases

Recent clinical studies have provided advances in diagnosis and treatment of cystic fibrosis, and new and greater emphasis now is

being placed on basic biochemistry, genetics and molecular biology research.

One investigator, in one of the first examples of "molecular therapy," (expected to be the treatment of the future in some inherited metabolic diseases) has successfully transplanted specific enzyme-producing cells into rats jaundiced because of a hereditary enzyme deficiency. After transplant the rats developed a normal capacity to handle bile. This unique biological model has potential implications for treating some types of inborn errors of metabolism. Current Institute research seeks to learn the metabolic defect or defects in cystic fibrosis and other metabolic diseases so the flaws may be corrected.

Endocrinology

The main thrust in endocrinology is to discover the precise mechanism by which hormones influence metabolism and other life processes and, thus, to gain better understanding of such disorders as hyperthyroidism, hypothyroidism, growth retardation and osteoporosis.

After 32 years of research, the human pituitary growth hormone (HGH) has now been synthesized by the same scientist who previously isolated and identified it. Another significant finding was synthesis of the active portion of parathyroid hormone and extension of knowledge of how it controls calcium metabolism.

These accomplishments have important implications for improved diagnosis and treatment of a number of endocrine disorders.

Kidney Diseases and Artificial Kidneys

Preliminary investigations revealed that dihydrotachysterol, a compound structurally similar to vitamin D, arrests the secondary hyperparathyroid bone disease that characteristically accompanies chronic kidney failure and, in many cases, chronic hemodialysis. Other studies indicate that the androgenic hormone, testosterone, may be of therapeutic value for anemic uremia patients on regular hemodialysis.

Among recent achievements is the development of a new generation of compact artificial kidneys, the so-called "hollow fiber dialyzers." These unique devices have been given extensive clinical tests and commercial production began this year. A number of other improved artificial kidneys are being developed.

Digestive Diseases and Nutrition

Peptic ulcer and other gastrointestinal disorders, and diseases of the liver and gallbladder are among the most common illnesses in this country. Recent research has established an association between the presence of a viral-like substance ("Australia antigen") and a type of hepatitis transmitted through blood transfusions or by contaminated needles. There is some evidence that fatal liver necrosis or cirrhosis occurs only in cases of acute viral hepatitis in which this antigen is present. It is anticipated that ongoing research eventually may permit development of a vaccine against hepatitis, or a therapeutically effective antibody preparation against the Australia antigen.

Investigators who earlier isolated a metabolically active form of vitamin D, 25-hydroxycholecalciferol (25-HCC), and showed that the liver is the principal site of vitamin D conversion into 25-HCC, now have obtained evidence that it is converted in kidney tissue to the ultimate biologically active form of vitamin D, namely 1,25 dihydroxycholecalciferol. Studies are under way to determine whether these active metabolites may provide a safe and effective treatment for vitamin D-resistant rickets.

Important findings have emerged from research in Southeast Asia to increase the protein level of rice, and from laboratory development of protein-rich food supplements. Among the latter is a new, modified, "extended" milk which is nutritionally equivalent to cow's milk but considerably cheaper. This promises to double the available milk supply for children in India.

Diseases of the Blood

Among Institute goals is elucidation of the specific defects in various types of anemia, such as sickle cell disease. A proposed new treatment has been devised for acute attacks of sickle cell anemia which makes use of urea, a common chemical. This therapy may reverse red blood cell sickling crises and block further sickling of susceptible red cells. The new approach is an outgrowth of the molecular theory of sickling advanced by an Institute scientist, who demonstrated that abnormal linkage occurs between certain hemoglobin chains in sickling-prone red cells.

National Institute of Child Health and Human Development

The National Institute of Child Health and Human Development during the past year placed particular research emphasis on population problems, child health, and the problems of the mature and aging adult.

Population Research

Our country's population has increased 50 percent in the past 30 years and is expected to increase another 50 percent before the year 2000. One cannot assess the impact of population growth without considering its effect on the health of children, families, and society as a whole. For example, avoiding unwanted births can significantly reduce infant mortality, prematurity, and mental retardation.

The Institute's Center for Population Research supports research and research training in three areas: new methods of fertility regulation, medical effects of current contraceptive methods, and social sciences aspects of population problems.

NEW CONTRACEPTIVE METHODS

No available contraceptive method is fully satisfactory. Institute research seeks to develop new ones. The activity has become product-oriented and by the end of the year will include drug development, from synthesis through clinical testing, to develop several new methods of fertility regulation. The Institute also supports directed basic research in reproductive biology.

MEDICAL EFFECTS OF CURRENT BIRTH CONTROL METHODS

Past studies suggest a variety of undesirable or adverse effects of present contraceptive methods. Attention has been directed toward precise documentation of conjectured associations between oral contraceptives and diseases such as thromboembolism and cancer. Epidemiological studies were continued of stroke, other thromboembolic diseases and cancer of the breast and cervix in women of reproductive age. Analysis in one study demonstrated the importance of demographic factors in interpreting pathological effects. New studies were begun to develop information about the metabolism of hormonal contraceptives and possible effects of their long-term use on carbohydrate and lipid metabolism, blood coagulation, blood pressure regulation and the effects of other common drugs.

POPULATION RESEARCH IN THE SOCIAL SCIENCES

Research continued on the ways social, economic, and psychological factors influence fertility. A constellation of projects examining the relationship between female roles and fertility will shed light on why persons desire and have different numbers of children and why other couples have unplanned children.

The National Fertility Study of American Women is the latest and most sophisticated of a series of surveys started in 1955 to facilitate analysis of changing population dynamics.

RESEARCH AND TRAINING

The Institute launched this year a long-term commitment to support Population Research Centers throughout the country. The new effort provides funds to universities and nonprofit institutions to conduct biomedical and behavioral research and research training on population issues.

The Population Research Center Awards (PRCAs) provide core support for facilities and services that might be unavailable to individual investigators. Progress is accelerated by providing pooled facilities to cooperating investigators, including computers, electron microscopes, assay and histologic laboratories, and testing facilities.

Funds are also available for developing new research and recruiting professional staff.

Child Health

Institute research is organized to eliminate conditions that prevent mothers from bearing healthy babies, to improve infant care and nutrition, and to prevent or ameliorate abnormalities that cause mental retardation.

IDENTIFICATION OF GENETIC DEFECTS IN THE FETUS

Most pregnant women express fear of having a defective child. Prenatal diagnosis may alleviate this fear and offer hope for preventing mental retardation and other handicapping abnormalities arising from genetic defects. Amniocentesis, a technique which involves drawing off a small amount of fluid surrounding the fetus, offers the opportunity for prenatal diagnosis. In collaboration with seven medical centers, the Institute is developing an amniocentesis registry to assess the safety of this procedure and determine if it is being used in the best interest of parents and society.

GROWTH AND NUTRITION

Children with severe malnutrition requiring hospitalization in the first year of life are found, three or four years later, to be shorter, weigh less, have small head circumference and a lower developmental quotient than children of the same age who are not malnourished. If malnutrition continues beyond the first four months, the child is more likely to display defective intellect later in childhood. Studies are underway to determine how severe malnutrition must be to produce intellectual deficits and at what stage it is the most devastating.

MENTAL RETARDATION

As with a child's physical development, the growth of his mental capabilities begins with genetic factors he inherited from generations before him. These are molded, sometimes irrevocably, by the forces of his prenatal environment, by the events surrounding birth and adjustments to postnatal existence, and thereafter by how these experiences interact with the nutritional and environmental conditions throughout his lifetime. All these developmental variables are being studied by scientists supported by the Institute.

The complexity of the problem of mental retardation has been highlighted in a detailed study in a selected community. Almost three percent of the children studied were found to be mentally subnormal. Of these, one-half showed definite signs of neurologic damage. The study demonstrated that children born to parents who themselves have been inadequately housed, nourished, and educated are at risk to prenatal, perinatal, and postnatal hazards. The combined interaction of these produces mental retardation in a substantial portion of those who survive.

Adult Development and Aging

The Institute's adult development and aging program is geared to improving the health of aging citizens, and thereby reducing the cost of their care.

Operant conditioning techniques have been used to change and control voluntary skeletal muscle action. Investigators at the Institute's Gerontology Research Center have found, for example, that some patients with abnormal heart rhythms can learn to control these abnormalities and maintain control after leaving the hospital, thereby improving their health and activity.

National Institute of Dental Research

Dental Caries

An intensified attack on tooth decay was launched in Fiscal Year 1971 by the National Institute of Dental Research as the result of an added \$5 million appropriation by the Congress.

Known as the National Caries Program, this targeted research effort has drawn vigorous response from the academic community and industry. In addition to its principal component of contracted research, the program includes expanded studies by Institute scientists and grant-supported investigators.

The program is designed to speed development of measures to prevent tooth decay, a universal affliction of children. Since caries is too complex a problem to yield to a single "magic bullet," a combination of measures is sought to depress the three interacting causative factors of the disease—susceptibility of teeth, carbohydrate-rich diet, and caries-inducing bacteria.

Current projects relate to improved methods of applying fluoride to teeth, the use of adhesive sealants to prevent caries on the chewing surfaces, and clinical testing of the enzyme dextranase as an anti-caries agent. Companion studies are directed toward better understanding of tooth structure and of oral bacteria which appear to be involved in the causes of caries.

In recent research, for example, branching filamentous (thread-like) bacteria were identified as important suspects of human tooth decay below the gum line. These organisms are not the same as those responsible for decay of crown surfaces. While table sugar (sucrose) may contribute to crown and root decay, starches and other sugars appear to be important in root caries. In other studies high concentrations of cadmium, lead, and zinc in soil and water have been associated with high rates of decay and delayed eruption of teeth.

Target for the 70's

At the request of the Appropriations Committees of the U.S. House of Representatives and the Senate, the NIDR Director submitted a five-year plan for the optimum development of the Nation's dental research effort. "Oral Disease: Target for the 70's" reviews the state of knowledge for the important oral-facial diseases and prospects for improved therapy, control, and ultimate prevention.

Dental Repair, Biomaterials

Improved biomaterials are continuously sought to repair damage between discovery and use of new substances, test procedures have been developed recently for alloys, plastics, and other materials, using implants in animals and by tissue cultures.

Another significant advance relates to dental amalgam, used for 80 percent of the fillings in this country. Substituting a little gold for silver in the amalgam makes it stronger and less likely to corrode. In other tests, a carboxylate cement has been shown to adhere to teeth so much better than traditional zinc phosphate cement that it is expected to prevent leakage around fillings and to make orthodontic bands practically obsolete.

Periodontal (Gum) Disease

This affliction is the chief cause of tooth loss after age 35. Research seeks a scientific base on which effective methods of therapy and prevention can be built.

The most prevalent form of periodontal disease, characterized by inflammation, is believed closely associated with bacteria that colonize on the teeth and gum tissues in an adherent film called plaque. As more is learned about these plaque-forming organisms and mechanism of adhesion, scientists believe effective methods of control and prevention can be developed.

Recent studies show that endotoxins released from dead bacteria in pockets around the teeth may enter the gums and cause plasma cells in nearby lymph nodes to make antibodies against them. Subsequent exposure to the endotoxins triggers local immune responses which contribute to the redness, swelling, and discomfort of periodontal disease. A clearer picture of the causes of oral-facial anomalies also emerges from past studies in this mystifying field.

Research to improve the rehabilitation of victims of cleft lip and cleft palate is continuing. Maxillo-mandibular surgery for certain caused by oral diseases. To improve safety and shorten the lag types of malocclusion has increased.

Pain and Anesthesiology

Irregular heartbeats, which may be a patient-management problem in adults during general anesthesia, can be largely prevented through prior administration of moderate doses of propranolol. Scientists also found that meprobamate is better than most muscle relaxants for pain in the hinge of the jaw since it is also a tranquilizer and can relieve pain that reflects subjective or emotional problems.

National Institute of Environmental Health Sciences

During the past year, Institute scientists made exciting progress in developing techniques for work in mutagenesis, utilizing the opossum for combination teratogenesis-carcinogenesis studies, in developing a microwave exposure system and techniques for diagnosing central nervous system toxicity of mercury and other metals.

Mutagenesis

SCREENING OF CHEMICALS FOR MUTAGENESIS

Repair of genetic damage before it causes irreparable change appears to constitute the principal means by which genes are properly maintained and protected from harmful environmental influences. Employment of a system in which each step of repair is individually assessed would reveal which chemical and physical agents interrupt and uncouple the sequence of repair. Such interruptions could conceivably cause more damage than the initial lesion. For instance, repair enzymes might produce multiple breaks in DNA and yet be prevented from resealing them by exogenous environmental influences.

By comparing the mutability of ultraviolet-resistant to ultraviolet-sensitive cells, NIEHS researchers hope to discover whether repair-replication contributes to the processes of mutagenesis.

DEVELOPING TECHNIQUES FOR WORKING IN MUTAGENESIS

In the past half century an unknown number of actual and potential mutagens—physical, chemical and biological—have been created and dispersed. To avoid long-term disastrous effects of rapidly accumulated mutations within any population, methods are needed which aid in detection and control of mutagens.

Systems to detect mutagens exist; each has limitations in sensitivity, ease of operation and relevance to man. NIEHS scientists are developing a mouse-mouse host-mediated assay for chemical mutagens which combines convenience and high sensitivity with biological relevance to mammals.

The scientists also developed a two-dimensional thin-layer chromatographic procedure useful for locating specific bases and chemical groups that react with potential mutagens.

This should facilitate studies of the interrelationships between dosimetry and toxicity and mutagenesis, and should be useful in

identifying specific base alterations that give rise to mutagenic lesions.

Teratogenesis-Carcinogenesis

The newborn marsupial is in many respects a fetus that completes its development in an extra-uterine environment. Only in marsupials is it possible to expose embryonic tissue directly and simply to toxic or physical insult. A systematic survey of the response of the marsupial to drugs and toxicants is not available. Such a study should yield new insight into the response of embryonic tissue to toxic insult.

Under conditions established at the Institute, animals of known age can be produced in large numbers making it possible for the first time to utilize a marsupial, the opossum, as an experimental animal for toxicologic and pharmacologic studies.

Investigation of the susceptibility of newborn marsupials to tumor induction by a chemical carcinogen shows that the animal develops several kinds of tumors as early as three months after exposure. Of greater interest, however, is an apparent association between developmental defects and tumors in many of the animals.

Microwave Exposure System

With increased use in tracking, communications, commercial products such as microwave ovens, and medical diathermy, microwaves have now become an environmental health problem. There is very little information concerning the effects of low-level, long-term exposure to microwave radiation. Much of the research on the biological effects of microwaves has been carried out in fields of unknown characteristics.

NIEHS scientists have developed and installed a generating system which operates at 2450 MHz with a power range of 0.01 to 200 mW/cm². The well-defined, uniform field has been calibrated three dimensionally and is used for developing dosimetry techniques and exposing biological systems. Studies are underway to determine thermal and other effects of microwave exposure to various test systems.

CNS Toxicity of Metals

Little is known about the devastating central nervous system disorders which result from methyl mercury poisoning. NIEHS physicians and veterinarians began examining the pathologic changes which follow ingestion of the metal.

The scientists are interested in the mechanisms by which mercury affects the brain, kidney, liver, spleen and other organs. They are attempting to relate blood and tissue concentration to toxicity. Biochemists are studying the effects on cell components and enzyme systems, and pharmacologists are examining its effects on fetal development in animals. It is hoped this approach will lead to improved diagnosis and to methods to reverse and repair the tragic results of methyl mercury.

National Institute of General Medical Sciences

Administration

The National Institute of General Medical Sciences this year, led by its new Director, Dr. DeWitt Stetten, Jr., launched a large new effort in basic and human genetics that will contribute to alleviation of inherited disease. The thrust in genetics resulted partly from the ripeness of this field, and from the conviction of Congress that genetic science should be more fully exploited.

NIGMS programs of research training and fellowships constitute a foremost resource for developing basic biomedical investigators and medical school faculty. Training is supported in 20 different disciplines. Standards for competence in these fields require, on the average, seven years of intensive graduate study and professional development. The quantity of students aided by the Institute therefore must relate to long-term medical faculty needs, evolving national priorities and public demand. Each of the 14 training committees which advise the Institute undertook an in-depth survey of their fields during the year. In most areas it was determined that current levels of support are not likely to produce an excess of scientist-teachers for the foreseeable future. For others it was ascertained that acute shortages of personnel probably will persist, and in a few fields it was found that training should be continued at approximately the present level.

Research Progress

GENETICS

Inherited diseases and disabilities are known to affect seriously some 15 million Americans. Many are fatal during the first few years of life. Thus far there is no lasting cure for any genetic disorder. Research has, however, begun to offer hope that genetic disease can be controlled by better diagnosis, treatment and prevention.

Congress this year recognized the magnitude of genetic disease as a public health problem, and appropriated \$7.75 million of added funds in support of 159 research projects. These brought to 361 the number of studies supported in genetics and genetic chemistry, and the Institute's total obligation for the year increased from \$28.50 million to \$36.25 million.

A key objective is to discover basic knowledge. One Institute grantee discovered the basic genetic defect in Tay-Sachs disease, a defective gene which normally codes for an enzyme needed to degrade certain fatty substances in the body. The disease occurs mainly in Jewish families of East European descent. Affected infants appear normal at birth but exhibit neural damage by age nine months and die by age 4.

The research makes it possible to test for the enzyme in blood samples from prospective parents and determine whether they carry a single gene trait for the disease. Persons who have only one defective gene do not manifest disease, but when two carriers mate, the risk is that one-fourth of their offspring will inherit the disorder. By contrast, there is no risk when a carrier is mated to a non-carrier. Accordingly, numerous Jewish communities have voluntarily commenced screening programs to identify carrier individuals and permit informed decisions regarding marriage and family planning to lessen the incidence of Tay-Sachs disease and perhaps, in time, prevent its transmission entirely. The same test also has been applied prenatally to fetal cells obtained by amniocentesis. Parents known to carry the disease trait have learned early in a pregnancy whether their child would have the disease.

Another discovery is a way to test in culture the leukocytes or white blood cells of potential donors and host recipients for skin and organ transplatation purposes. The test reveals the prospective donor whose tissues are most compatible to the host and less likely to be rejected. In one recent use of the test to select donors a two-year survival rate of 95 percent was reported for a large group of kidney transplant patients. The result is perhaps double the expected level with less sensitive techniques.

FUNDAMENTAL SCIENCES

The Institute supports fundamental studies in bio-organic chemistry and enzymology, and on cell structure and function. During the year a grantee discovered that the metal, molybdenum, is a vital cofactor for the enzyme, sulfite oxidase. Man is increasingly exposed to sulfur dioxide, an atmospheric pollutant. Sulfur dioxide is changed to sulfite in the body and toxic concentrations can build up unless it is degraded by sulfite oxidase. Therefore a deficiency of molybdenum could result in a deficiency of sulfite oxidase, increasing the risk of injury.

AUTOMATED CLINICAL LABORATORIES

Advances were made in biomedical engineering and medical laboratory technology to increase the accuracy and speed of diagnostic

tests. The prototype for a new generation of fast analyzer instruments was evaluated clinically at Georgetown University Hospital, Washington, D.C. Used daily over a period of eight months, the machine performed as many as 50 blood or urine chemical determinations precisely and reliably in a matter of minutes. Patients could be treated during a single visit on the basis of completed laboratory data instead of having to return later. Analytical error was more than two percent, compared to 10 to 15 percent for conventional instrumentation.

PHARMACOLOGY-TOXICOLOGY

Scientists at the University of Rochester demonstrated the effectiveness of a new resin as a binding agent for methyl mercury. Mice fed the resin in their diet and given injections of methyl mercury excreted the mercury three times more rapidly than did control animals. This may permit the resin to be given orally to counteract mercury poisoning in man.

Clinical studies showed that harmful effects of L-dopa on the heart can be eliminated by the concurrent use of another drug, propranolol, or by gradually increasing the dosage of L-dopa over a long period. This finding has implication in the treatment of parkinsonian patients, treated with L-dopa, who may be prone to heart disease.

Other investigators showed that a widely used anticonvulsant drug given to pregnant mice produces cleft palate in their young.

TRAUMA

Two new trauma research centers were established, one in Mississippi and one in Massachusetts, bringing to nine the number supported by NIGMS. Accidental injuries each year kill more than 116,000 Americans and permanently disable another 400,000. In these centers both basic and clinical studies are conducted on biochemical, physiological and systemic responses to injury.

One basic study suggests that the hormone glucagon improves blood flow to abdominal tissues without increasing heart output. If confirmed in patients, it might be possible to administer the hormone to help prevent "stress ulcers" in the stomach, a frequently fatal consequence of trauma and major surgery.

National Institute of Neurological Diseases and Stroke

Research Trends

The National Institute of Neurological Diseases and Stroke directs much of its research toward finding the cause and prevention of disease. This is especially important since effective treatment is not available for most chronic neurological conditions.

Tremendous progress has been made, for example, in diagnosing, even before birth, a group of hereditary lipid-storage disorders, most of which cause severe mental retardation. Tests for carriers of the defective gene and of the unborn fetus have been developed for nine of these diseases. There is now an excellent prospect that these disorders can be eliminated from the population within the foreseeable future.

Information provided by the Institute's Collaborative Perinatal Research Project is helping reduce the number of children suffering from neurological disorders arising during the perinatal period (from conception to 28 days after birth). The study showed that certain viruses in the mother, once thought harmless, can lead to neurological damage in the newborn. It was found that several drugs taken during pregnancy can cause congenital malformations and stillbirth, and that diabetes is related to the frequency of birth defects in the offspring. Perhaps most important is the discovery that maternal weight gain during pregnancy can have a significant effect on the birthweight of the infant and his development.

Among the serious neurological conditions arising during childhood are the convulsive disorders such as epilepsy. Many afflicted now have their seizures controlled by drug therapy and lead normal lives. Drug therapy can benefit an even larger number through effective monitoring of blood levels and patient response to an antiepileptic agent by gas-liquid chromatography. This technique—once limited to research laboratories—has become increasingly available to practicing physicians, in large part due to the Institute's epilepsy program.

Disorders of the Aged

Although three-fourths of all neurological disorders arise in the perinatal period, others begin late in life. Increasing numbers of Americans, for example, are moving into the age groups menaced by stroke and Parkinson's disease.

An urgent problem is improvement of acute stroke care, since 70 to 80 percent of deaths occur within the first 10 days. Institute research findings recently indicated that the brain can survive regional losses of circulation for longer periods than previously believed. This finding leads to the hope that the effects of a stroke may be overcome if circulation can be quickly restored in the affected areas. NINDS has therefore launched a pilot study of acute stroke care.

Until the goal of stroke prevention can be achieved, reduction of deaths and serious disabilities due to strokes must depend on more effective treatment. The Institute therefore made plans to establish at least six multi-disciplinary acute-care research units to test and monitor the status of the nervous system and to evaluate new methods of medical and surgical intervention.

Better instrumentation must be developed for monitoring acute stroke victims and for diagnosis of incipient strokes. Promising new possibilities for improved measurement of cerebral blood flow are ultrasound and nuclear magnetic resonance devices.

In Parkinson's disease, another condition affecting older persons, relief for many patients is available. It is now clear that L-dopa has revolutionized treatment for many of the more than one million people in the U.S. who are afflicted with this severely crippling disorder. Clinical studies must be continued to determine why some patients do not respond to L-dopa treatment, to develop adequate dosage methodology, and to try to control the rather serious side effects.

Development of L-dopa therapy, which has brought relief to thousands suffering from Parkinson's disease, now promises even greater dividends in new research opportunities. Several new projects have been launched utilizing L-dopa to explore the chemistry, physiology and pharmacology of the brain. As an important by-product of this research, for the first time there is hope for effective treatment of other diseases of abnormal movement, such as Huntington's chorea and dystonia musculorum deformans.

Sclerosing Disorders

The Institute has also increased its efforts against the sclerosing disorders, the most common of which is multiple sclerosis. Institute research led to the discovery that three neurological conditions are caused by a transmissible agent. Institute scientists have stepped up the search for a virus as the possible cause. A world-wide tracking operation, coordinated by NINDS, is being conducted to isolate

transmissible agents. In this collaborative study, a large number of known viruses also are being screened in animal tests.

Over 100,000 persons in the Nation are paralyzed in the arms, legs, or both due to spinal cord injury. Preliminary data suggest that if the acute injury is properly treated, the degree of permanent damage can be lessened and, in some cases, nearly complete function reestablished. Improved methods of diagnosing and treating acute injuries are needed.

Spinal Cord Injuries

To find solutions to this serious problem, the Institute made plans to establish four Acute Spinal Cord Injury Clinical Research Centers. Within these many disciplines will cooperate in developing techniques for emergency care at the place of accident or injury. The centers will also conduct studies for improved emergency room diagnostic techniques and medical-surgical treatment.

Most common of all neurological problems are the handicapping communicative disorders which afflict 20 million Americans. The Institute supports nearly 300 research projects and five multi-disciplinary clinical research centers on hearing and speech disorders and special problems such as aphasia. In order to accelerate research on the biological effects of noise and its relationship to hearing loss, the Institute is setting up a Laboratory of Neuro-otolaryngology and will support eight outpatient deafness research centers. In an unusual but important project, the Institute has undertaken the difficult medico-legal problem of the definition of death. Because mechanical life-support devices—such as the pacemaker to maintain the heart beat and the respirator to sustain breathing—are now widely used, traditional criteria for death are no longer valid. A device to calibrate and test automatically all channels of EEG apparatus used in evaluation of cerebral death has been developed.

Clinical Center

The Clinical Center continued to provide clinical research facilities and services for the National Institutes of Health to assure that patients received the finest care and treatment while participating in research protocols, and to provide opportunities for young physicians and other professionals to prepare for careers in medical or related research or in academic medicine.

Patient Load and Care

During the year, patient admissions numbered 4,466, an increase of 123 over the previous year. Readmissions for followup totaled 3,285, an increase of 158. Outpatient clinic visits jumped from 32,049 to 38,197.

The average length of stay decreased slightly to 26 days, in contrast to 29 days in 1970 and 31 days in 1969. Bed occupancy rate averaged 63 percent. The total number of patients admitted to the Clinical Center from July 6, 1953 through June 30, 1971, was 62,692.

Despite increased workload demands, more complex procedures, and a 10-20 percent rise in the cost of supplies, the Clinical Center was able to maintain its tradition of specialized, quality patient care.

This was accomplished through judicious selection of priorities; intensive education and training of para-medical personnel as well as advanced courses for professional staff; greater reliance on assistance from hospital volunteers; and maximum utilization of automation systems and pre-packaged, disposable products.

Diagnostic Radiological Services

Capitalizing on a gradual build-up of capabilities, diagnostic radiological services supported many research projects. In this category were the bone and lung biopsies and bronchial brushing under fluoroscopic visualization; catheterization and blood sampling of any artery or vein that can receive a catheter with relative safety; and ultrafine polytomography of any structure.

Also cineradiography and videotape recording and other special diagnostic procedures which greatly advance clinical research information.

Automated Laboratory Procedures

Important steps were taken to perform a greater volume and variety of tests in the computer-assisted automated laboratory, and to provide faster test results to attending physicians.

For example, an early ward report system was instituted and programs were written to generate a discharge summary of any patient's laboratory data, as well as a statistical summary of all laboratory tests on a monthly basis.

Elective Courses

A new program of elective courses for medical students was inaugurated early in Fiscal Year 1971. The staff of several Institutes and the Clinical Center collaborated to provide instruction in three clinical subspecialties—Endocrinology, Hematology, and Immunology—and Computers in Clinical Medicine.

Nineteen students participated. The students were rotated through the various clinical wards, and attended special lectures and rounds.

Associate Training Program

Administrative support and coordination of the NIH Associate Training Program was continued, and 202 of the 522 applicants were selected to participate in the program in 1972, following a year of residency training.

Division of Biologics Standards

Diploid Cell Lines

Viral vaccines have been important factors in raising the quality of life in the United States over the past two decades, with the introduction of vaccines for the prevention of poliomyelitis, measles, mumps, and rubella. The success associated with their use depends both on the vaccines themselves, and upon their careful control. The agency responsible for controlling all biological products shipped in interstate commerce or imported into the United States is the Division of Biologics Standards (DBS).

Efforts are directed toward continued monitoring for safety, purity, and potency of products now on the market, and toward application of new knowledge to improve biologics and to develop new ones.

Of particular interest has been evaluation of cell substrates used in producing viral vaccines. As a result, research is being directed toward development of non-human diploid cell strains, to serve as alternatives for primary cell cultures and to increase assurance of safety.

Two promising non-human primate diploid cell strains have been developed under contract. Both meet the criteria of acceptability for vaccine production, including cytogenetic and growth characteristics, freedom from adventitious agents, and ability to support the growth of viruses. The strains have been made available to interested virologists and commercial establishments for further evaluation.

Hepatitis Research

Hepatitis constitutes a serious risk in the administration of blood and blood products. Transfused blood is known to cause more than 30,000 cases of hepatitis every year in the U.S., of which 10 percent are fatal.

The Division of Biologics Standards has for many years maintained an exploratory program of hepatitis research. This was expanded in 1968 to keep pace with findings which linked the Australia antigen with hepatitis. This antigen appears to be related, or may actually be the cause of serum hepatitis. Thus for the first time, specific tests for presence of a hepatitis virus in blood are available.

During the year the DBS has evaluated test procedures in blood-donor screening for detection of hepatitis-associated antigen

(HAA). Information was acquired on HAA-positive blood donors, and a panel of blood donor serum specimens was established for evaluating additional tests as they are developed. The studies show that by eliminating positive HAA donor blood, serum hepatitis cases could be reduced by as much as 25 percent.

In addition, the DBS was involved with standardizing materials with which the tests are performed, and which are subject to licensure through DBS. Federal regulations for specific standards of safety, purity, and potency for the antisera—hepatitis-associated antibody (anti-Australia antigen)—were developed by the DBS this year, and four manufacturers were licensed for commercial distribution of the materials. Steps were begun to amend Federal regulations to require that all blood collected for transfusion or further processing be tested for hepatitis-associated antigen. Only negative blood will be used.

Division of Computer Research and Technology

The rapid incorporation of computing into the substance of the NIH programs continued in 1971.

Facilities and Services

Use of central NIH computing resources grew vigorously. The work stream increased 112 percent to 87,000 jobs per month. Both the interactive terminals and the remote job entry terminals in the network almost doubled to 250 and 18, respectively. Interactive terminal sessions more than doubled to 1,000 per day. This growth was supported by new elements and reconfigurations of the Computer Center system. These include three processors instead of four, a new single job queue for all processors, a shared on-line data storage area of more than a billion bytes capacity, and program-controlled optical character reading.

Systems Development

Other computer systems were developed for specific NIH laboratory environments and incorporated into biomedical research. Research applications on the central computers moved ahead with the addition of new generating software to provide programs tailored to individual needs. New emphasis was given during the year to chemical and biological information systems for research in carcinogenesis, transplantation, immunology and heart disease. A collaborative development began with the NIH Clinical Center for the creation of more extensive and integrated clinical care systems.

Research Developments

DCRT research in its own laboratories and in conjunction with other laboratories spanned the biomedical spectrum from the physical-molecular to the clinical levels, and from use of laser, nuclear magnetic and other techniques for analysis of molecules and cells to improvement in treatment of myocardial infarction, cancer, immune disorders and other diseases. An international working conference on "Cerebellar Modelling" was conducted, and hardware models of neurological networks were developed. DCRT also made advances in research in fundamental computer science, including

automatic question-answering and problem solving, automatic induction and pattern recognition, and balanced-tree algorithms.

Education

In addition to continuing education of NIH staff to use computers efficiently and effectively, the DCRT provided a Computer Operator Training Program for a group of NIH employees to move from dead-end jobs into new careers.

Division of Research Grants

The Division of Research Grants responsibility in administering policy on protection of human subjects in research was broadened to include all DHEW agencies and expanded to include all subjects at risk. Regional meetings with representatives of grantee institutions proved a productive method for disseminating information to grantee and contractor personnel responsible for implementing the policy, and for gaining understanding of their problems in developing local criteria and controls.

A Priority Score Review Committee, established to study the initial review group priority score system, recommended adoption of a special formula to normalize raw priority scores given to applications recommended for approval. The new system became effective July 1, 1971.

A Study Section for Population Research was established to handle the growing number of applications in that field.

All study sections took steps to note neglected areas of research. Several workshop-conferences were sponsored to assess the status of research and to stimulate further studies where need was evident. Among these, the Hematology Study Section held a conference on sickle cell disease to stimulate research and improve patient care, after more than a year of planning. Similarly, the Nutrition Study Section sponsored a workshop on "Nutritional Anemias" to assess research on metabolic relationships between folic acid and vitamin B₁₂ on iron metabolism and on tocopherol deficiency.

A workshop attended by scientists, including members of the Developmental Behavioral Sciences Study Section, and laymen representing minority groups, was held to consider problems of achievement in society, and to examine ways in which minority group members can perceive and seek higher levels of achievement. It was expected the conference would reveal problems worthy of research in the social sciences.

A comprehensive computer system for the *Research Grants Index* was put into operation for storage and automatic search and retrieval of information about research projects supported by the Public Health Service.

The Training Opportunity Program Committee extended its area of interest to employee problems and equal employment opportunity. The Director assigned to this group a broader range of Equal Employment Opportunity advisory functions.

Division of Research Resources

In Fiscal Year 1971, the Division of Research Resources once again became an independent research Division within the NIH as a result of a reorganization in the Bureau of Health Manpower Education. This change allowed the Division greater managerial flexibility, in addition to providing closer rapport with the other research components of NIH.

Biotechnology Resources

In November 1970, the Special Research Resources Branch was renamed the Biotechnology Resources Branch, better reflecting the nature of its work. The branch supports computer centers and resources in gas chromatography/mass spectrometry, high voltage electron microscopy, and nuclear magnetic resonance spectroscopy.

During FY 1971, the branch developed the resource-related grant mechanism as a means of improving research services available at resources not funded by NIH. Under the grant, scientists are programming computers to predict automatically the structure of complex organic compounds in the body (such as steroids) from their mass spectrograms, or "chemical signatures." This service will be available to all users.

General Clinical Research Centers

Each of the 80 Division-supported general clinical research centers is a small research hospital, located within a large medical complex, where researchers can intensively study diseases, their causes, and their treatment.

For example, in recent years, scientists have shown that one area of the brain, the hypothalamus, secretes hormones that act on the pituitary gland, stimulating it to release other hormones. These pituitary hormones in turn stimulate the thyroid, adrenals, ovaries, and testes to produce their respective hormones. Within the past year, researchers at a GCRC for the first time isolated and synthesized one of the hypothalamic hormones, thyrotropin-releasing-factor (TRF). TRF may provide the basis for precise, safe, and sensitive tests for early diagnosis of pituitary gland problems.

Animal Resources

At one laboratory animal resource supported by the Division, scientists successfully transmitted lepromatous leprosy—the most

severe form—to a nine-banded armadillo. The success offers hope of establishing the armadillo—a bizarre, prehistoric-looking mammal found throughout much of the south—as a model for study of a disease which affects 15 million persons in the world.

Also, during the year, a team of researchers at a Division-supported primate center showed for the first time that owl monkeys can develop a form of leukemia similar to that commonly seen in children. The researchers said the monkeys will provide a model for drug treatment of this disease. Earlier, in the year, the same team received the highest award of the American Association for Laboratory Animal Science for related viral-cancer work.

General Research Support

In a pilot project under a General Research Support Grant, a rechargeable cardiac pacemaker was invented the past year. This transistorized device can be recharged through the skin, eliminating periodic surgery to replace conventional batteries. The device was selected as one of the 10 outstanding U.S. inventions of 1970.

Division of Research Services

The Division of Research Services continued to provide NIH researchers with direct support in biomedical engineering and instrumentation, environmental services, medical library services, medical arts and photography, animal production and care, and media production. The Division's Equal Employment Opportunity efforts resulted in gains in hiring blacks and other minorities in higher-level positions, as well as increased training and new career opportunities.

Environmental Services

Increased concern with environmental quality was reflected in establishment of three committees directly related to the Environmental Services Branch. These are: The Inter-Institute Committee on Biohazards; The Coordinating Safety Council; and the Ad Hoc Committee on Environmental Differential Pay. In addition, a report on environmental working conditions at NIH was prepared.

Training for select NIH employee groups was increased in scope and number. Ten new courses were developed.

Biomedical Engineering and Instrumentation

Study was concentrated on analytic aspects of pharmacokinetics in brain injury, hemodialysis, and cancer chemotherapy. Concepts of thermodynamics and chemical kinetics, with computer simulation, were used to aid in antineoplastic drug therapy, hemodialysis, and brain edema studies.

Animal Programs

Dedication ceremonies were held in May for a new Primate Building at the NIH Animal Center in Poolesville, Maryland. The facility is designed for quarantine, conditioning, and breeding of up to 1,500 nonhuman primates.

Although only a few months old, the Animal Disease Investigation Service (ADIS) has been well received by investigators and is contributing toward improvement of animal health. A number of disease conditions were investigated and controlled, often after detailed multi-disciplinary study. The information gathered will be useful to the biomedical research community in general.

Library Services

The NIH Library implemented a new Library Services Adviser program to broaden integrated bibliographic and reference services. The Library's response to requests may now utilize substantial external resources, such as specialized information centers, computerized information retrieval systems, and clearinghouses.

Medical Arts and Photography

The Medical Arts and Photography Branch streamlined methods and instituted new and improved technology, such as a computer graphics service capable of large scale production. Over \$60,000 in contracted work was required to handle the increase in requests for color photographic and art services. Funding of still photography services was switched to the NIH Revolving Fund on April 1.

The Fogarty International Center

Scholars-in-Residence

During Fiscal Year 1971 the John E. Fogarty International Center for Advanced Study in the Health Sciences continued to fulfill its mission as a focal point for advanced study by outstanding scholars from abroad. The following Scholars were in residence: Prof. Torsten Teorell, Sweden, Prof. John Edsall, United States, Prof. Isaac Berenblum, Israel, Prof. Jeffries Wyman, Italy, Prof. Rollin Hotchkiss, United States, and Prof. Ruggero Ceppellini, Italy.

Each Scholar pursued his own studies; in some cases this included the writing of a book, or conducting seminars, workshops and lectures. Typical activities included a seminar series on allosteric interactions by Professors Edsall and Wyman sponsored in cooperation with the National Institute of Arthritis and Metabolic Diseases.

Conferences and Seminars

Eight conferences were held on these topics: Reform of Medical Education II; Role of Research in Medical Education; Radionuclide Applications in Hematology; Periodontal Disease in Puberty and Adolescence; The Regulation of Mammalian Reproduction; Transfer RNA and Carcinogenesis; Oral Sensation and Reception; Glycoproteins with Hormonal Activity; and Prospects in Gene Therapy.

At the conference on the Role of Research in Medical Education, the discussions strongly suggested that good medical training cannot be imparted to students without exposing them to the experimental method. The conference on Regulation of Mammalian Reproduction successfully identified promising areas of research for development of new techniques in fertility regulation. One of the most productive conferences was that on Transfer RNA and Carcinogenesis. Transfer RNA (tRNA) has a central role in translation of the genetic code and protein synthesis. This conference concentrated on studies relevant to the functional role of tRNA in protein synthesis and how this applies to cell differentiation and the cause of cancer.

Bilateral Agreements for Cooperation

During Fiscal Years 1969 and 1970, efforts were undertaken to develop biomedical cooperation within existing or newly negotiated

bilateral general science agreements which encourage cooperating governments to share the cost of research and research training. Under these agreements, several biomedical exchanges have taken place between American and biomedical scientists from Australia, the Republic of China, France and Italy. This cooperation was continued. In addition, an agreement was signed between the United States and Spain.

Under the U.S.-U.S.S.R. Agreement an exchange of biomedical delegations took place to consider organ transplants.

Geographic Health Studies

The Fogarty International Center initiated a Geographic Health Studies effort. One of the components of this, the Soviet Health Studies Project, resulted in the publication of three documents, including: *The Soviet Five Year Plan for Public Health, 1971-1975*; *Fundamental Principles of Health Legislation of the U.S.S.R.*; and *Soviet Medical Research Priorities for the Seventies*.

Studies involving health in other countries including Sweden and the Peoples Republic of China, were in progress.

Bureau of Health Manpower Education

ADMINISTRATIVE CHANGES

The Bureau was reorganized and renamed the Bureau of Health Manpower Education. Three Divisions remained essentially the same—Dental Health, Nursing, and Allied Health Manpower. Newly established were the Divisions of Physician and Health Professions Education with Dr. Harry W. Bruce as the Director, and Manpower Intelligence with Dr. William A. Lybrand as Director.

DPHPE is concerned with all aspects of education of physicians, osteopaths, dentists, optometrists, pharmacists, podiatrists, and veterinarians. Activities include administration of institutional grants to increase the number of health professionals and to improve the quality of their education, construction grants for educational facilities, and student scholarships and loans.

The Division of Manpower Intelligence develops, interprets, and analyzes information on national health manpower supply and demand, and includes a National Clearinghouse for Health Manpower Information.

Dr. Daniel F. Whiteside, a former Division Director, was appointed Associate Director of the Bureau to coordinate grants policy. An Office of Program Planning and Evaluation was established with Dr. Eugene A. Confrey as chief.

The Bureau emphasized activities to attract disadvantaged personnel into the health manpower field.

An agreement between the Bureau and the National Library of Medicine, created an Office of Audiovisual Educational Development at the National Medical Audiovisual Center in Atlanta, Georgia, to develop better instructional and training materials.

LEGISLATIVE DEVELOPMENTS

Public Law 91-519 the Health Training Improvement Act of 1970, was enacted on November 2, 1970. Title I provided funds to assist medical and dental schools in financial difficulties and modified institutional grants to be responsive to new health professions schools. Title II authorized improvement and strengthening of allied health professions training through June 30, 1973.

Bureau funding rose from \$373,405,068 in FY 1970 to \$420,151,413 in 1971; the number of permanent, full-time employees declined from 742 to 737.

Division of Allied Health Manpower

ALLIED HEALTH TRAINING

Allied health professions training in 335 junior colleges, colleges, and universities was strengthened by educational improvement grants totaling \$9,701,000. Enrollment in schools awarded the grants increased by 3,329 students over the 1970 level to 26,166.

Grants totaling \$3,347,168 were awarded to 81 public and private nonprofit agencies, organizations and institutions to support advanced training of allied health professionals preparing for positions as educators, administrators, supervisors and non-research specialists. Grants for advanced training of less than an academic year were initiated.

Grants and contracts for special projects for training allied health personnel were initiated. They incorporated previous grants to develop curricula for new types of health manpower. A total of \$4,971,713 was awarded in 76 Special Project Grants.

PUBLIC HEALTH TRAINING

The number of schools of public health rose to 17 with the opening of a new one at the University of Washington in Seattle. Division grants for curriculum development totaled about \$9.5 million, with about half of this sum divided on a formula basis among the 17 schools. The remainder went to 186 projects in graduate public health training.

Traineeships totaling \$8.4 million were awarded to approximately 8,000 students enrolled in full-time academic training and short courses in public health nursing, preventive medicine and dentistry and the public health aspects of nutrition, population planning, hospital/health services administration, engineering, and environmental health.

NEW SPECIAL ACTIVITIES

Operation MEDIHC (Military Experience Directed Into Health Careers)

The National Office for the DHEW-DOD MEDIHC program was established in the Division. More than 5,000 veterans with health skills requested assistance in locating employment and training opportunities in the health field in order to utilize their military experience.

Minority

The Division initiated two contracts directed at problems in education that affect the quality and the supply of non-white personnel in allied health professions.

Under the contracts, the Urban League is studying the training potential in traditionally non-white colleges, and the Charles R. Drew Postgraduate Medical School in Los Angeles is developing a health manpower training center to supply health services needed in that area.

Division of Dental Health

CARIES PREVENTION

The Division continued public education activities in support of community water fluoridation. As of December 31, 1970, fluoridation reached some 92 million people nationwide: 83,725,771 have access to water supplies with a fluoride content adjusted to optimum level and another 8,500,000 enjoy naturally fluoridated water. Seven states have enacted laws requiring fluoridation.

TEAM

New Training in Expanded Auxiliary Management (TEAM) grants funded eight projects totaling \$695,000. These supplemented and succeeded the previous Dental Auxiliary Utilization (DAU) grants. These awards emphasize the role of the dentist as manager of a total dental health team and greatly increase the role of dental auxiliaries in dental care.

DENTAL MANPOWER DEVELOPMENT CENTER

The Dental Manpower Development Center in Louisville, Ky., site of a recently completed 5 1/2-year dental productivity study, has been redesigned to serve as an experimental clinical training center. The new facilities will allow use of experimental dental auxiliary training curricula, modern learning environments and clinical facilities. The DMDC's new role is the intramural portion of the TEAM effort.

"DR. DIAL"

The Dental Health Center, San Francisco, Calif., provided technical assistance to a model six-week health education project in Casper, Wyo., on prevention and control of periodontal disease. Mass communication channels were employed to inform the public. Approximately 60 percent of the patients who had dental appointments during the period reported they were familiar with the "Dr. Dial" project; 14 percent made their appointments because they had been reminded by "Dr. Dial" of the consequences of dental neglect. Based on the success in Casper, plans are being made to conduct similar efforts in other communities.

CONTINUING DENTAL EDUCATION

Continuing dental education for practitioners received renewed emphasis by the Division. Projects were either started or planned to promote regional information systems for dentists, emphasizing education television networks and participative clinical sessions. Minnesota, Iowa, Nebraska, North Dakota and South Dakota operated the first system.

GRANT AWARDS

Twenty-six project grants totaling \$1,244,000 were awarded; included was support for analysis of preventive dental behavior and cultivating positive attitudes among dental students toward team practice. Four research training grants totaling \$445,000 supported training in the fields of dental health education and socio-dental research. Nine fellows and two career development awardees received support totaling \$150,000.

Division of Manpower Intelligence

The Division's activities were largely concerned with developing its organization, recruiting personnel, and implementing steps to meet long-range as well as immediate objectives.

ACCOMPLISHMENTS

Effort was centered on improving existing management information systems and new data gathering procedures, analysis and dissemination on all aspects of health manpower.

Seventy computer programs were created, tested and documented, among them Modification of the data base established for the Bureau construction grants information system to include HPEA (Health Professions Educational Assistance) payment and anticipated application data.

The Division now serves as the source of Bureau grant and loan data for the IMPAC (Information for Management Planning, Analysis, and Coordination) System maintained by the Division of Research Grants.

CONTRACTS

In addition to identifying areas where existing information is inadequate, the Division awarded contracts to acquire needed data on specific health manpower problems. These included surveys on characteristics of unsuccessful medical applicants, student and faculty interaction, distribution of black physicians, and socio-economic characteristics of licensed laboratory personnel. Contracts were initiated for feasibility studies to develop information systems for pharmacy, podiatry, and optometry manpower.

Division of Nursing

Activities to combat the nursing shortage and improve nursing practice emphasized aid to students and schools of nursing as authorized by Title II of the Health Manpower Act of 1968. These included contracts for recruitment of minority students and men into nursing; research and training to qualify nurses for expanded roles; acquisition and dissemination of new information about nursing manpower; and consultation to help State groups meet nursing requirements.

AID TO STUDENTS

Representative new special project grants kept 7 financially distressed schools from closing, assisted 4 more to offer remedial training for minority students, helped 24 to establish or plan nursing courses, and enabled an additional 5 to train nurses for expanded roles. A collegiate nursing curriculum established with Division funds in rural Arizona is tailored to needs of students with academic and cultural deficits. A project at the University of California at Davis is qualifying experienced public health nurses as independent providers of family-oriented health services with training in diagnostic assessment, family planning and pediatrics, clinical management of acute and chronic diseases, and threats to family health.

Sixteen construction grants totaling \$10.5 million were made.

An estimated 30,000 undergraduate and graduate nursing students received \$34 million in loans and scholarships. Traineeship grants totaling \$9,700,000 enabled an estimated 2,700 nurses to prepare for supervisory, teaching, and nurse specialist responsibilities.

A \$100,000 contract was awarded to the 50,000-member National Student Nurses' Association to give national support to "Break-through to Nursing," a project to recruit student nurse volunteers, including males and students from minority groups. Contract funds were awarded to the Wisconsin Higher Education Aids Board to provide minority high school students and Indian Americans in the 20-40 age range remedial instruction essential for acceptance into nursing schools.

RESEARCH AND RESEARCH TRAINING

A training contract was awarded the University of North Carolina for research in applying epidemiological principles to program planning and evaluation. One study documented a positive relationship between lack of prenatal care and prematurity, infant mortality, and maternal anemia.

Research grants supported 55 projects. Nurse Fellowship and Nurse Scientist training grants aided 286 nurses prepare for research in 30 health-related fields.

STATE PLANNING AND MANPOWER STUDIES

Division consultation helped nursing leaders in 10 States design and act on plans to overcome State deficits in manpower and other nursing resources. The Division supported the first national inventory of licensed practical nurses which resulted in publication of the only comprehensive reference on L.P.N. supply and distribution.

Division of Physician and Health Professions Education

NEW SPECIAL ACTIVITIES

A Division contract study on the semiannual admissions system of the University of Tennessee College of Medicine was completed. It showed the plan nearly doubles the number of yearly graduates compared with conventional single-class admissions.

The University of Miami School of Medicine received support to re-train persons with Doctor of Philosophy degrees in science to become Doctors of Medicine. The two-year training plan is one of several new approaches to relieving the physician shortage.

Division funds were provided to the American Foundation for Negro Affairs of Philadelphia to formulate a four-year premedical curriculum to give minority students improved access to schools of medicine and health sciences.

EDUCATIONAL IMPROVEMENT AWARDS

The Division awarded 270 institutional grants to schools of medicine, osteopathy, dentistry, pharmacy, veterinary medicine, optometry, and podiatry in the total amount of \$46,800,000.

Awards of 163 special project grants were made to the same types of schools in a total amount of \$100,550,000, including \$23,000,000 for physician augmentation and \$400,000 for Dental Auxiliary personnel. These grants led to an increase of nearly 1,000 first-year places in medical and dental schools.

STUDENTS ASSISTANCE

The Division allocated \$25,000,000 for health professions loans to an estimated 22,000 students in 252 participating schools. Health professions scholarships were allocated in the amount of \$15,500,000 to 269 schools for an estimated 18,000 students.

HEALTH PROFESSIONS EDUCATIONAL FACILITIES

Matching construction funds totaling \$126,565,795 were awarded to 24 participating schools, enabling them to increase their capacity by 681 new first-year places. Of this amount, \$82,285,240 provided 405 new places in 14 schools of medicine, \$25,786,781 added 80 new places in 5 schools of dentistry, and \$18,493,774 provided 196 new places in 5 schools of optometry, podiatry, pharmacy, or veterinary medicine.

National Library of Medicine

The National Library of Medicine, this year observing both the 135th anniversary of its founding in 1836 by the Army's first surgeon general and the 10th anniversary of the dedication of its unique and functional building, continued to expand its developing biomedical communications network of regional medical libraries and supporting activity.

The success of the on-line, experimental remote bibliographic service, known as AIM-TWX, in use by about 50 institutions since June 1970, led to its further development. A contract was awarded for third-generation computer equipment for MEDLARS (Medical Literature and Analysis System). This conversion is to add expanded vocabulary and design features to coordinate MEDLARS and the AIM-TWX system. This action followed a decision not to continue the MEDLARS II as negotiated in June 1969.

The Library's Presidentially-appointed Board of Regents established a Scholars-in-Residence plan to encourage and recognize scholarly research requiring use of the Library's collection.

Library Operations

All of the 11 Regional Medical Libraries were operational by September 1970 and the network processed more than half a million requests for interlibrary loans. More than 125,000 of these were filled from the MEDLARS data base which now exceeds 1.4 million bibliographic citations. There was an increase of 26 percent in the number of demand literature searches for domestic users.

Five new recurring bibliographies were initiated, bringing the total produced by the Library to 23. The monthly *Abridged Index Medicus*, begun in 1970, continued to be well received. More than 2.7 million pages of deteriorating and replaceable material were microfilmed to archival standards. New acquisitions raised the total of the Library's collections to 1,347,521 titles.

Planned as a prototype for other medical libraries, a basic multimedia resource area was completed in the main reading room. The new facility includes soundproof viewing rooms, a color television receiver with earphones, microfiche and microfilm readers, a cassette recorder, conventional slide and film projectors and a stereophonic tape recorder. More than 1,000 titles are listed in the card catalog of the multimedia collection.

Lister Hill National Center for Biomedical Communications

In June 1970, the Center began testing an experimental two-way closed circuit television link between the Dartmouth University Medical School and the Claremont General Hospital, about 30 miles distant. The project was designed to extend the consultation facilities of a university medical center to physicians in a somewhat isolated area. An auxiliary link was made available three hours daily for transmission of electrocardiograms. An additional contract was completed to include the University of Vermont in the network.

In addition to improving the AIM-TWX system, the Center continued to develop satellite communication experiments to improve health care services in Alaska. A two-level network between participating university clinical centers and the Alaskan Native Medical Center to field service units will be extended to 26 villages in areas with unreliable short wave radio reception. The network will permit direct consultation between physicians, and also between physicians and health aides in the villages.

Specialized Information Services

Toxicology Information Services were expanded through collaborative access to automated data banks and systems of the Food and Drug Administration and the Environmental Protection Agency that contain pesticide data. Through an agreement with the Atomic Energy Commission, a Toxicology Information Query Center was established at the Oak Ridge National Laboratory. This permits in-depth searches from literature of many scientific disciplines and most commercial literature tape services. A new on-line, computer-based *Roster of Authorities in Specialized Subtopics of Toxicology and Related Fields* became operational.

National Medical Audiovisual Center

The Center cooperated with several organizations in producing audiovisual instructional units for medicine, dentistry, nursing and related health professions. Modularly constructed teaching packages were developed for cross-sharing among 28 member schools of the Association of Deans of Southern Medical Schools. A slide/sound package on the team approach to dentistry was produced in cooperation with the Division of Dental Health of the Bureau of Health Manpower Education, and successfully used in training

dental faculty. The Bureau created an Office of Audiovisual Educational Development at the Center.

In the first full year of a computer-supported distribution system, the Center processed about 120,000 requests and loaned 85,000 audiovisuals. The International Index of Medical Film Data was reviewed to maintain currency, and its 25,000 citations reduced to 4,000. During the year, 10 seminar/workshops were presented by the staff, and three others were co-sponsored with national organizations.

Extramural Support

The Medical Library Assistance Extension Act of 1970 enabled the Library to make 529 awards for \$5,992,000. Specialized manpower training support in 17 training categories assisted 112 persons pursuing health information studies.

The amended resource grant authority attracted 462 applications during the year as compared to 594 received during the five year authority of the Medical Library Assistance Act of 1965. Contracts were negotiated and awarded to 7 of the 11 operating Regional Medical Libraries.

The Library continued to sponsor a series of projects in Israel, Poland and Yugoslavia under special foreign currency (Public Law 480) agreements.

NATIONAL INSTITUTES OF HEALTH APPROPRIATIONS FISCAL YEAR 1971

(In thousands of dollars)

	TOTAL	RR ¹	NIAID	NIAMD	NCI	NICHD	NIDR	NIEHS	NIGMS
Total-----	\$1,688,799	\$66,201	\$102,249	\$138,339	\$230,383	\$94,436	\$35,257	\$20,620	\$166,072
Grants-----	861,217	63,288	71,417	111,523	110,977	64,701	23,321	13,099	153,777
Research-----	671,490	62,810	58,274	90,003	95,605	50,773	16,269	9,048	88,553
Fellowships-----	49,964	126	3,749	5,740	3,798	3,786	1,601	264	18,454
Training-----	139,763	352	9,394	15,780	11,574	10,142	5,451	3,787	46,770
Direct Operations-----	335,032	2,913	30,832	26,816	119,406	29,735	11,936	7,521	12,295
Direct research-----	106,406	---	17,167	17,548	20,658	9,102	5,833	6,696	---
Biometry & epidemiology-----	9,060	---	---	858	---	2,145	670	---	---
Collaborative studies-----	182,303	---	---	---	---	---	---	---	---
Biologics standards-----	8,838	1,384	11,794	5,915	94,739	15,350	4,333	---	7,665
Training-----	661	---	93	---	---	73	---	---	268
Review and approval-----	19,239	909	1,452	2,157	2,792	2,178	724	456	3,209
Program direction-----	6,710	620	326	338	1,217	887	376	369	1,153
International center-----	1,815	---	---	---	---	---	---	---	---
Health Manpower Education ² -----	431,131	---	---	---	---	---	---	---	---
Health manpower-----	275,934	---	---	---	---	---	---	---	---
Dental health-----	11,014	---	---	---	---	---	---	---	---
Construction grants-----	141,100	---	---	---	---	---	---	---	---
Loan funds-----	3,083	---	---	---	---	---	---	---	---
National Library of Medicine-----	20,769	---	---	---	---	---	---	---	---
Office of the Director-----	8,206	---	---	---	---	---	---	---	---
Buildings and Facilities-----	---	---	---	---	---	---	---	---	---
Scientific Activities Overseas ³ -----	32,444	---	---	---	---	---	---	---	---

¹ Formerly General Research and Services (GR&S); now Research Resources.

² Formerly Bureau of Health Professions Education and Manpower Training (BHPEMT); now Bureau of Health Manpower Education.

³ Special foreign currency program (PL 480) included in NIH budget for administrative purposes.

NATIONAL INSTITUTES OF HEALTH APPROPRIATIONS FISCAL YEAR 1971

(In thousands of dollars)

	NHLI	NINDS	DBS	FTC	BHME ²	NLM	NEI	OD	B&F	SAO ³
Total	\$193,479	\$105,807	\$8,838	\$3,582	\$431,131	\$20,769	\$30,986	\$8,206	-----	\$32,444
Grants	141,288	79,513	-----	1,767	-----	-----	26,546	-----	-----	-----
Research	116,774	61,759	-----	650	-----	-----	20,972	-----	-----	-----
Fellowships	6,871	2,782	-----	1,117	-----	-----	1,676	-----	-----	-----
Training	17,643	14,972	-----	-----	-----	-----	3,898	-----	-----	-----
Direct Operations	52,191	26,294	8,838	1,815	-----	-----	4,440	-----	-----	-----
Direct research	16,413	11,182	-----	-----	-----	-----	1,807	-----	-----	-----
Biometry & epidemiology	1,807	3,250	-----	-----	-----	-----	330	-----	-----	-----
Collaborative studies	30,491	9,300	-----	-----	-----	-----	1,332	-----	-----	-----
Biologics standards	-----	-----	8,838	-----	-----	-----	-----	-----	-----	-----
Training	165	62	-----	-----	-----	-----	658	-----	-----	-----
Review and approval	2,690	2,014	-----	-----	-----	-----	313	-----	-----	-----
Program direction	625	486	-----	-----	-----	-----	-----	-----	-----	-----
International center	-----	-----	-----	1,815	-----	-----	-----	-----	-----	-----
Health Manpower Education ²	-----	-----	-----	-----	431,131	-----	-----	-----	-----	-----
Health manpower	-----	-----	-----	-----	275,934	-----	-----	-----	-----	-----
Dental health	-----	-----	-----	-----	11,014	-----	-----	-----	-----	-----
Construction grants	-----	-----	-----	-----	141,100	-----	-----	-----	-----	-----
Loan funds	-----	-----	-----	-----	3,083	-----	-----	-----	-----	-----
National Library of Medicine	-----	-----	-----	-----	-----	20,769	-----	-----	-----	-----
Office of the Director	-----	-----	-----	-----	-----	-----	8,206	-----	-----	-----
Buildings and Facilities	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
Scientific Activities Overseas ³	-----	-----	-----	-----	-----	-----	-----	-----	-----	32,444

Formerly General Research and Services (GR&S); now Research Resources.

² Formerly Bureau of Health Professions Education and Manpower Training (BHPEMT); now Bureau of Health Manpower Education.

³ Special foreign currency program (PL 480) included in NIH budget for administrative purposes.

NIH GRANTS AND AWARDS BY COMPONENT AND PROGRAM, FISCAL YEAR 1971¹

(Amounts in millions of dollars)

NIH component	Total amount	Research grants ²		Research contracts		Research training grants		Research fellowships and traineeships		Research career awards		Education ⁴ grants		Construction grants		Medical library grants	
		Num-ber	Amount	Num-ber	Amount	Num-ber	Amount	Num-ber	Amount	Num-ber	Amount	Num-ber	Amount	Num-ber	Amount	Num-ber	Amount
Total -----	\$1,414.2	11,063	\$676.2	1,350	\$155.3	2,134	\$131.4	2,913	\$24.9	1,169	\$28.1	3,214	\$258.8	43	\$137.1	471	\$2.5
Institutes and Research Divisions --																	
NIAMD -----	996.5	10,959	671.6	1,186	144.6	2,111	129.2	2,718	23.8	1,167	27.9	—	—	—	—	—	—
NIAMD -----	72.8	1,164	51.5	135	8.4	163	8.8	96	0.9	110	2.7	—	—	—	—	—	—
NIAMD -----	107.6	2,054	81.9	66	5.1	294	15.0	222	2.3	135	3.4	—	—	—	—	—	—
NIAMD -----	173.7	1,214	88.4	387	70.8	187	10.8	191	1.8	83	2.0	—	—	—	—	—	—
NIAMD -----	75.7	844	46.9	197	15.1	131	10.0	100	0.9	123	2.9	—	—	—	—	—	—
NIAMD -----	24.9	230	16.1	37	2.1	98	5.3	68	0.7	28	0.6	—	—	—	—	—	—
NIAMD -----	13.1	120	9.5	6	0.8	43	3.1	12	0.1	6	0.1	—	—	—	—	—	—
NIAMD -----	24.6	446	19.2	6	0.8	51	3.0	65	0.9	26	0.8	—	—	—	—	—	—
NIAMD -----	141.8	1,137	77.8	7	2.4	525	43.4	1,358	9.7	392	8.7	—	—	—	—	—	—
NIAMD -----	161.5	1,707	109.8	238	27.5	380	17.6	157	2.1	177	4.7	—	—	—	—	—	—
NIAMS -----	77.5	1,394	53.7	69	7.0	230	11.8	299	3.1	87	2.0	—	—	—	—	—	—
NIAMS -----	118.7	649	116.8	11	1.4	9	0.4	12	0.1	—	—	—	—	—	—	—	—
NIAMS -----	1.2	—	—	—	—	—	—	138	1.2	—	—	—	—	—	—	—	—
NIAMS -----	1.6	—	—	21	1.6	—	—	—	—	—	—	—	—	—	—	—	—
NIAMS -----	0.2	—	—	8	0.2	—	—	—	—	—	—	—	—	—	—	—	—
NIAMS -----	2.0	—	—	8	2.0	—	—	—	—	—	—	—	—	—	—	—	—
Bu. Health Manpower Educa. -----	407.4	67	3.7	111	5.6	13	1.3	191	1.0	2	(⁵)	3,214	258.8	43	137.1	—	—
OD -----	0.9	—	—	35	0.9	—	—	—	—	—	—	—	—	—	—	—	—
DAHM -----	36.1	15	—	15	1.1	—	—	—	—	—	—	1,066	35.0	—	—	—	—
DDH -----	5.8	23	0.9	12	0.6	4	0.3	8	0.1	2	(⁵)	69	3.9	—	—	—	—
DMI -----	0.7	—	—	12	0.7	—	—	—	—	—	—	—	—	—	—	—	—
DN -----	71.9	35	2.0	28	1.7	9	1.0	183	0.9	—	—	—	55.9	16	10.5	—	—
DPHPE -----	292.0	9	0.8	9	0.6	—	—	—	—	—	—	—	694	27	126.6	—	—
Nat. Lib. Med. -----	9.7	37	0.9	53	5.4	10	0.9	4	0.1	—	—	—	—	—	—	471	2.5

¹ Excludes scientific evaluation grants.

² Includes general research support programs.

³ Includes NINDS traineeships.

⁴ Includes institutional grants (formula), special project grants, and awards for student assistance.

⁵ Less than \$50 thousand.

NOTE: Dollars may not add due to rounding. Supplemental grants are combined with parent grants or with other supplements when both awards are financed from the same fiscal year's funds.

NATIONAL INSTITUTES OF HEALTH EMPLOYMENT BY COMPONENT, JUNE 30, 1971

Component	(Perma- nent full-time) 1970	Compar- ison between fiscal years 1970-1971	(Perma- nent full-time) 1971
Total.....	11,138	+114	11,252
Office of the Director.....	¹ 1,888	+5	1,893
National Institute of Allergy and Infectious Diseases.....	676	-11	665
National Institute of Arthritis and Metabolic Diseases.....	588	+9	597
National Cancer Institute.....	1,355	+71	1,426
National Institute of Child Health and Human Development.....	415	+20	435
National Institute of Dental Research.....	283	+6	289
National Institute of Environmental Health Sciences.....	202	+18	220
National Eye Institute.....	85	+7	92
National Institute of General Medical Sciences...	180	-16	164
National Heart and Lung Institute.....	558	+26	584
National Institute of Neurological Diseases and Stroke.....	588	-5	583
Clinical Center.....	1,443	+18	1,461
Fogarty International Center.....	48	-1	47
Division of Biologies Standards.....	263	+1	264
Division of Computer Research and Technology..	284	-3	281
Division of Research Grants.....	425	-8	417
Division of Research Resources.....	82	+1	83
Division of Research Services.....	572	-20	552
Bureau of Health Manpower Education.....	742	-5	737
National Library of Medicine.....	461	+1	462

¹ Includes NIH Central Services and Program Direction functions.

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